

中文題目：血糖差悖論：重症患者是否存在相對低血糖之現象？

英文題目：Paradox of Glycemic Gap: Does Relative Hypoglycemia Exist in Critically Ill Patients?

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Background: High glycemic gap, mainly caused by stress-induced hyperglycemia, was reported to be a predictor of increased mortality in critically ill patients. However, the impact of hypoglycemia among the same population was also well-documented. We aimed to investigate the effect of different levels of glycemic gaps on the mortality rates, and to determine whether low glycemic gap is associated with worsen outcomes in critically ill patients.

Methods: We retrospectively screened 2678 patients admitted to the medical or surgical intensive care units (ICUs) during December, 2015 to July, 2017. After excluding patients with absolute hypoglycemia, extreme hyperglycemia, or with incomplete glycemic records, 935 patients were enrolled for analysis. A1C-derived average glucose (ADAG) and glycemic gaps were calculated for each patient. Patients were further classified into 5 groups according to their glycemic gap obtained at ICU admission (very low, low, medium, high, and very high). Confounding factors such as age, APACHE II score, major comorbidities, and causes of ICU admission were evaluated. All patients were followed up for one year, or till the occurrence of mortality.

Results: Patients with very low glycemic gaps were with lower serum glucose, higher HbA1c levels, higher prevalence of diabetes, and with higher disease severity. Compared to patients with medium glycemic gap, both patients with very low (HR: 1.786, 95% CI: 1.166-2.735, $p=0.008$) and very high (HR: 1.623, 95% CI: 1.057-2.269, $p=0.027$) glycemic gaps were associated with higher one-year mortality. However, only subjects with very low glycemic gaps were significantly associated with higher one-year mortality (adjusted HR: 1.665, 95% CI: 1.079-2.571, $p=0.021$) in the multivariate regression. The significant association was observed even in the subgroup analysis.

Conclusion: Our study suggested that low glycemic gap during ICU admission, which implied relative hypoglycemia, was independently associated with higher one-year mortality. The importance of relative hypoglycemia among critically ill patients should be emphasized in clinical practice.

Keywords: A1C-derived average glucose; glycemic gap; hypoglycemia; intensive care units

Table 1. Basic characteristics of patients grouped by different levels of glycemic gaps while admission to intensive care units (ICU)

	Very low (n=187)	Low (n=187)	Medium (n=187)	High (n=187)	Very high (n=187)	P value
Age	66.86±15.25	68.02±16.44	67.44±17.01	69.48±16.45	69.83±13.44	0.291
Gender (male)	128(68.45)	135(72.19)	123(65.78)	117(62.57)	104(55.61)	0.227
BMI	23.81±4.82	24.74±4.35	24.93±5.86	23.69±4.42	24.83±4.83	0.024
APACHE II scores	24.33±8.76	22.71±8.49	24.30±8.48	24.36±8.15	26.30±7.74	0.005
Glycemic profiles						
Glycemic gap	-50.07±41.57	5.98±10.96	42.63±10.75	84.44±16.69	189.35±62.77	<0.001
Glucose	125.93±46.58	146.36±42.81	184.69±41.11	230.83±50.18	331.77±71.45	<0.001
HbA1c	7.57±2.00	6.52±1.40	6.58±1.35	6.73±1.62	6.59±1.45	<0.001
Cause of ICU admission						
Respiratory failure	77(41.18)	73(39.04)	64(34.22)	72(38.50)	78(41.71)	0.862
Shock	38(20.32)	33(17.65)	39(20.86)	38(20.32)	42(22.46)	
Post-operation/PCI	43(22.99)	48(25.67)	51(27.27)	49(26.20)	46(24.60)	
Others	29(15.51)	33(17.65)	33(17.66)	28(14.97)	21(11.23)	
Comorbidities						
Hypertension	109(58.29)	114(60.96)	118(63.10)	96(51.34)	108(57.75)	0.194
Diabetes	148(79.14)	114(60.96)	121(64.71)	137(73.26)	157(83.96)	<0.001
Dialysis	23(15.51)	21(11.23)	26(13.90)	25(13.37)	23(12.30)	0.789
Cirrhosis	9(4.81)	14(7.49)	11(5.88)	16(8.56)	22(11.76)	0.107
Heart failure	32(17.11)	32(17.11)	26(13.90)	24(12.83)	19(10.16)	0.249
CAD	33(17.65)	55(29.41)	40(21.39)	38(20.32)	36(19.25)	0.055
Stroke	18 (9.63)	15 (8.02)	8 (4.28)	14 (7.49)	23 (12.30)	0.076
Malignancy	51(27.27)	45(24.06)	50(26.74)	53(28.34)	49(26.20)	0.915
Sepsis	83(44.39)	80(42.78)	74(39.57)	85(45.45)	100(53.48)	0.089
Medications						
OAD	69(36.90)	46(24.60)	56(29.55)	67(35.83)	69(36.90)	0.040
Insulin	39(20.86)	21(11.23)	22(11.76)	36(19.25)	47(25.13)	0.001
Statin	42(22.46)	40(21.39)	39(20.86)	36(19.25)	31(16.58)	0.656
Steroid	20(10.70)	17(9.09)	18(9.63)	18(9.63)	14(7.49)	0.875
Data at ICU admission						
WBC (k)	12.07±8.90	11.16±7.03	10.70±4.79	11.29±6.51	11.82±7.31	0.448
Hemoglobin	9.80±2.26	10.15±2.19	10.00±2.19	9.68±2.25	9.84±2.18	0.301
Creatinine	2.79±2.66	2.55±2.47	2.92±2.79	2.91±2.87	2.66±2.19	0.609
ALT	168.10±666.88	85.38±232.55	81.38±163.74	144.87±336.38	147.63±338.47	0.289

BMI: body mass index, ICU: intensive care units, HbA1c: Hemoglobin A1c, PCI: percutaneous coronary intervention, OAD: oral antidiabetes drugs, CAD: coronary artery disease, WBC: white blood cell, ALT: Alanine aminotransferase

Figure 1. (A) Changes of glyceimic profiles, (B) incidence of mortality, and (C) the Kaplan-Meier curves in patient group by different levels of glyceimic gaps.

