



- Under steady state for sodium-glucose co-transporter-2 inhibitor (SGLT-2 inhibitor) in type 2 diabetes (T2D), it has been reported that decreased 1-h mean glucose levels is associated with decreased 1-h urine glucose levels [1].
1. Nakamura Y, et al. *Expert Opin Pharmacother*. 2015; 16: 2553-9.
- There is little information regarding prediction abilities for urine glucose levels in eGFR and mean glucose levels.
- We studied regarding the relationship between blood glucose and urine glucose levels in T2D patients who had reached steady state upon taking a SGLT-2 inhibitor.

● Ten patients with T2D taking Luseogliflozin 2.5 mg for more than 2 weeks were hospitalized for diabetes treatment.

● During hospitalization, the patients wore a continuous glucose monitor (CGM: iPro2) for 6 days (CGM attachment: day 1) while continuing Luseogliflozin 2.5 mg intake.

● All other antidiabetic treatments were adjusted to improve glycemic variability.

● From day 2 to day 5, starting from 9 AM, we obtained four consecutive 24-hour mean blood glucose levels (24-h MGL) and 24-hour urine glucose levels (24-h UGL), respectively.

● “24-h MGL and 24 h-UGL during the same period” (paired MUGL) were compared.

● We arranged paired MUGL in descending order of 24-h MGL. Then, consecutive 20 paired MUGLs were selected while shifting selection start one by one.

● Estimated glomerular filtration rate (eGFR) was measured once during hospitalization.

● For each selected group, we used multivariate linear regression analysis to predict the 24-h UGL from the 24-h MGL and eGFR, where we commonly applied eGFR as a pair for the four paired MUGLs per each patient.

Simula tion	24-h MGL	eGFR	Rank	24-h MGL	eGFR	(n = 39)
Patient 1	150	85	1	250		Rank 1-20, n = 20
	145		2	245		Rank 2-21, n = 20
	130		3	240		Rank 3-22, n = 20
	120		⋮	⋮		⋮
Patient 2	180	45	18	180	45	Rank 18-37, n = 20
	190		19	175		Rank 19-38, n = 20
	170		20	170	45	Rank 20-39, n = 20
	155		⋮	⋮		⋮
⋮	⋮	⋮	37	120	85	
⋮	⋮	⋮	38	115		
⋮	⋮	⋮	39	110		

- Primary endpoints
 - Correlation between 24-h MGL and 24-h UGL
- Secondary endpoints
 - Standard partial regression coefficient (β) for eGFR, β for 24-h MGL, p for eGFR, p for 24-h MGL, adjusted- R^2 for a regression formula (RF), and p for RF when multivariate linear regression analysis is performed in the condition where the response variable is 24-h UGL and the covariates are 24-h MGL and eGFR, for each selected group
 - Correlation between mean of 24-h MGL and β for eGFR, β for 24-h MGL, p for eGFR, p for 24-h MGL, adjusted- R^2 for RF, and p for RF, in the selected groups
 - Correlation between patients and distribution of “24-h UGL \div (24-h MGL \times eGFR)” (U/MeG)

One paired MUGL was excluded from the analysis due to inaccurate urine glucose measurement. The arranged paired MUGL were numbered from 1 to 39 and consecutive 20 paired MUGLs were selected 20 times (from “1–20” to “20–39”: 20 groups).

A scatter plot showing the relationship between 24-h MGL (mg/dL) on the x-axis and 24-h UGL (mg/dL) on the y-axis. The x-axis ranges from 0 to 400 with major ticks every 50 units. The y-axis ranges from 0 to 140 with major ticks every 20 units. There are 39 data points represented by black dots. A dashed red line represents the linear regression. The text $n=39$ is in the top right corner, and $r=0.81, p<0.001$ is in the upper left area of the plot.

Table 2: Correlation between mean of 24-h MGL and values analyzed using multivariate linear regression analysis

β and Adjusted- R^2 : multivariate linear regression analysis

r (to Mean of 24-h MGL): Spearman's rank correlation coefficient

β , Standard partial regression coefficient; RF, regression formula

➤ Mean of 24-h MGL correlated with β for eGFR, β for 24-h MGL, p for eGFR, p for 24-h MGL, adjusted- R^2 for RF, and p for RF ($r=-0.61$, -0.76 , 0.72 , 0.62 , -0.62 , and 0.62 , respectively; $n=20$).

Patients correlated with distribution of U/MeG (correlation ratio: $\eta^2=0.71$, $p<0.001$).

The present study result suggests that, under steady state for SGLT-2 inhibitor in T2D, decreased 24-h MGL may be associated with decreased 24-h UGL. This result corresponds to the previous report [1].

➤ The present study results also suggest that increased 24-h MGL could lead to a reduced ability of predicting 24-h UGL using both 24-h MGL and eGFR.

➤ It has been reported that decreased eGFR reduces urinary glucose excretion action of SGLT-2 inhibitor [2, 3] and that chronic hyperglycemia increases SGLT-2 expression [4].

➤ In this study, the proportion of glucose levels derived from high SGLT-2 expression may have been higher in high MGL than in low MGL. High SGLT-2 expression can theoretically increase glucose levels relatively compared to UGL despite high eGFR. These may cause lower prediction ability in high MGL than in low MGL.

➤ SGLT-2 expression being different for each patient may be one of the influence factor on the present study result that patients correlated with distribution of U/MeG.

2. Ferrannini E, et al. Diabetes Care. 2013; 36: 1260-5.
3. Yale JF, et al. Diabetes Obes Metab. 2013; 15: 463-73.
4. Rahmoune H, et al. Diabetes. 2005; 54: 3427-34.

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