Serum 1,5-Anhydroglucitol Concentrations Are a Reliable Index of Glycemic Control in Type 2 Diabetes With Mild or Moderate Renal Dysfunction

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OBJECTIVE—To assess the relationship between 1,5-anhydroglucitol (AG) levels, which are a marker of glycemic control, and stages of chronic kidney disease (CKD).

RESEARCH DESIGN AND METHODS—This was a cross-sectional study with 269 subjects with type 2 diabetes who were divided into four groups based on estimated glomerular filtration rate (eGFR) using Modification of Diet in Renal Disease (eGFR$_{MDRD}$) formula: 57 in control, 111 in CKD stages 1–2, 78 in stage 3, and 23 in stages 4–5.

RESULTS—The study groups differed significantly with respect to 1,5-AG and fasting plasma glucose (FPG), age, duration of diabetes, blood pressure, HDL, and percentage of antihypertension or antidyslipidemia medication use. Stepwise multivariate regression analyses showed that 1,5-AG levels in the control group, the CKD stages 1–2 group, and the CKD stage 3 group could be explained by HbA$_{1c}$, age, duration of diabetes, FPG, and antihypertension medication. However, eGFR$_{MDRD}$ was the only independent determinant of 1,5-AG levels in CKD stages 4–5. Logarithmic transformed 1,5-AG values (ln[1,5-AG]) had significant inverse correlations with HbA$_{1c}$ and FPG levels for CKD stages 1–2 and CKD stage 3 (all $P < 0.001$). However, associations between ln(1,5-AG) and HbA$_{1c}$ or FPG were insignificant for CKD stages 4–5 ($P = 0.274$ and $P = 0.080$, respectively).

CONCLUSIONS—This study demonstrated that 1,5-AG levels do not appear to be influenced by mild or moderate renal dysfunction, suggesting it is a reliable glycemic marker in type 2 diabetes with CKD stages 1–3.

S trict glucose control in early stages of type 2 diabetes can result in significant clinical benefits, including reduced cardiovascular mortality (1) and improved renal function (2–4). Although HbA$_{1c}$ levels have been the main glycemic marker in the management of type 2 diabetes since the 1980s, other measures of glycemic control are available, such as glycated albumin, fructosamine, and 1,5-anhydroglucitol (1,5-AG). Compared with HbA$_{1c}$, serum 1,5-AG levels can reflect more recent glycemic control (5) as well as postprandial hyperglycemia (6).

Measuring 1,5-AG levels has several advantages, including retained metabolic inertness, steady-state levels in all tissues, and negligible influence of sampling conditions such as collection time, body weight, age, sex, and food intake of the subjects (7). However, 1,5-AG reabsorption is competitively inhibited in the renal proximal tubule by glucosuria and is excreted in the urine when glucose levels surpass the renal threshold for glucosuria (8,9). Studies have reported that values for 1,5-AG may be influenced by several physiologic factors or diseases associated with disturbed or impaired renal function (10–14), although these studies had small sample sizes. Little information is available on the relationship between 1,5-AG levels and the mild or moderate renal dysfunction commonly found in subjects with type 2 diabetes. Therefore, this study assessed the effects of renal function on the glycemic marker 1,5-AG in type 2 diabetes using classification by chronic kidney disease (CKD) stage.

RESEARCH DESIGN AND METHODS

Subjects and study design

A cross-sectional study was conducted involving individuals with type 2 diabetes who had serum creatinine and spot urine analyses during at least two visits over 3 months and who had 1,5-AG levels available at the Department of Endocrinology and Metabolism of Kangbuk Samsung Hospital in Korea between 2008 and 2010.

The estimated glomerular filtration rate (eGFR) was calculated by using the Modification of Diet in Renal Disease (MDRD) formula: eGFR$_{MDRD}$ = 186 × serum creatinine$^{-1.154}$ × age$^{-0.203}$ × [0.742 if female]. In accordance with the National Kidney Foundation Disease Outcomes Quality Initiative classification system, CKD was defined on the basis of eGFR and categorized into three groups defined by the cutoff points between stages 2 and 3 as well as between stages 3 and 4. Therefore, subjects in the stages 1–2 CKD group had eGFRs ≥60 mL/min/1.73 m^2, the stage 3 CKD group had eGFRs <60 to ≥30 mL/min/1.73 m^2, and the stages 4–5 CKD group had eGFRs <30 mL/min/1.73 m^2 (15). Subjects with an eGFR ≥90 mL/min/1.73 m^2 without proteinuria or history of kidney disease were placed in the control group. Consequently, 269 subjects were grouped as follows: 57 in control, 111 in

CKD stages 1–2; 78 in stage 3; and 23 in stages 4–5. Subjects with acute renal failure, recent infection, dialysis, known renal tubular acidosis, pregnancy, type 1 diabetes (C-peptide <0.18 nmol/L), chronic liver disease, or malignancy were excluded. Subjects aged <30 years or >70 years were also excluded due to the small number of participants in these age categories and potential comorbidities. The protocol for this study was approved by the institutional review board at Kangbuk Samsung Hospital. Written informed consent was obtained from all subjects.

Laboratory data

Levels of 1,5-AG were measured using an enzymatic assay with a two-reagent system, Determiner L 1,5-AG (Kyowa Medex, Tokyo, Japan). The assay was automated with an ADVIA 1800 Automatic Analyzer (Siemens, IL) according to the manufacturer's instructions. The measurement procedures, reference intervals, and coefficients of variation (CV) for 1,5-AG were based on previously published research (16).

HbA_{1c} levels were measured using high-performance liquid chromatography (Variant II, Bio-Rad Laboratories, Hercules, CA). The CV for glucose was <1.5% and the CV for HbA_{1c} was <3.0%. Serum creatinine was measured using the timed end point method (Unicel DxC 800, Beckman and Coulter, Krefeld, Germany). Urinary albumin and creatinine levels were determined using the DCA 2000 urinalysis device (Bayer Corp., Elkhart, IN). Intra-assay and interassay CVs were reported as being within the range of 2–8% for albumin/creatinine ratio. Serum insulin levels were measured using an immunoradiometric assay (Biosource, Nivells, Belgium) following the manufacturer's recommendations. Plasma lipids, including total cholesterol, triglycerides, and HDL and LDL cholesterol levels were measured by enzymatic colorimetric assay (Siemens, Tarrytown, NY).

Statistical analyses

Data are expressed as a median with range or number (proportions). Logarithmic transformations were applied to the 1,5-AG data before analyses. Baseline characteristics according to CKD stage were compared using a Kruskal-Wallis test with post hoc analyses or a χ^2 test. Skewed data, such as 1,5-AG values, were log-transformed for further analysis. Stepwise multivariate linear regression analyses were performed to identify the independent variables associated with logarithmic transformed 1,5-AG values (ln[1,5-AG]) values. To perform these analyses, demographic variables and continuous variables that were significantly different in baseline characteristics and significantly correlated with ln(1,5-AG) values in the Spearman correlations were included in the model. The model also included dummy variables, such as smoking status, and use of antihypertension and antidyslipidemia medication. Finally, the relationships between ln(1,5-AG) levels, HbA_{1c}, and fasting plasma glucose (FPG) levels were assessed for the control group and the three CKD categories using linear regression analyses. IBM SPSS Statistics 19.0 software (IBM, Armonk, NY) was

Table 1—Baseline characteristics of the subjects according to CKD stages

Variables	Control	CKD stages 1–2	CKD stage 3	CKD stages 4–5	P
n (%)	57 (21.2)	111 (41.3)	78 (29.0)	23 (8.6)	
Demographics					
Age (years)	54 (47–62)‡§	57 (51–62)‡	61 (56–64)*†	62 (52–68)*	<0.001
Women	26 (45.6)	37 (33.3)	36 (46.2)	9 (39.1)	0.258
Clinical characteristics					
Diabetes duration (years)	1.3 (0.8–5.0)†‡§	6.0 (2.0–10.0)*‡§	10.0 (4.0–15.0)*†§	15.0 (10.0–20.0)*†‡	<0.001
BMI (kg/m^2)	24.4 (22.7–26.8)	25.3 (22.8–27.7)	24.8 (23.2–26.7)	24.2 (22.5–25.8)	0.532
Current smoker	18 (31.6)	27 (24.8)	10 (14.7)	3 (23.1)	0.165
Laboratory data					
Serum creatinine (μmol/L)	61.9 (53–71)†‡§	80 (71–97)*‡§	115 (97–133)*†§	248 (221–292)*†‡	<0.001
eGFR$_{MDRD}$ (mL/min/1.73 m^2)	102 (98–109)†‡§	76 (69–88)*‡§	55 (46–59)*†§	22 (14–28)*†‡	<0.001
1,5-AG (μg/mL)	12.4 (5.5–17.6)‡§	8.1 (3.0–15.3)‡	1.7 (1.3–9.2)*†	3.9 (2.0–5.1)*	<0.001
FPG (mmol/L)	7.5 (6.9–9.2)§	8.3 (7.3–10.3)§	7.7 (6.6–9.1)§	6.5 (5.3–7.2)*†‡	<0.001
HbA$_{1c}$ (%)	6.8 (6.2–7.9)	7.4 (6.6–8.7)	7.4 (6.3–8.0)	7.8 (6.6–9.5)	0.071
Systolic BP (mmHg)	126 (116–137)†	134 (124–143)*	132 (120–143)	136 (130–150)	0.011
Diastolic BP (mmHg)	78 (73–89)‡	81 (74–91)‡	76 (66–81)*†	80 (73–89)	<0.001
Cholesterol (mmol/L)					
Total	4.8 (4.3–5.3)	4.7 (4.1–5.4)	4.5 (3.7–5.3)	4.3 (3.4–5.3)	0.214
HDL	1.2 (1.0–1.4)§	1.2 (1.1–1.4)‡§	1.1 (0.9–1.3)†	1.0 (0.8–1.2)*	<0.001
LDL	2.6 (2.1–3.1)	2.7 (2.2–3.3)	2.5 (1.8–3.4)	2.4 (1.5–3.0)	0.451
Triglycerides	1.8 (1.2–2.7)	1.5 (1.1–2.5)	1.7 (1.2–2.2)	1.5 (0.9–2.1)	0.720
Insulin (pmol/L)	64.5 (53.9–75.4)	66.2 (46.6–99.6)	64.0 (50.0–82.4)	47.4 (31.5–93.7)	0.433
C-peptide (nmol/L)	0.88 (0.70–1.02)	0.89 (0.68–1.10)	0.84 (0.67–1.10)	1.07 (0.63–1.62)	0.757
Presence of albuminuria	0 (0)†‡§	111 (100)*	37 (47.4)*	23 (100)*	<0.001
Urinary ACR (mg/g)	10 (7–15)†‡§	81 (50–174)*‡§	25 (8–143)*†§	376 (200–2,000)*†‡	<0.001
Medications					
Antihypertension	19 (33.3)	67 (60.9)	46 (59.7)	22 (95.7)	<0.001
Antidyslipidemia	9 (15.8)	38 (34.2)	35 (45.5)	13 (56.5)	0.001

Values are median with interquartile range or number (proportions). P value by Kruskal-Wallis test with post hoc analyses or χ^2 test. ACR, albumin-to-creatinine ratio; BP, blood pressure. *P < 0.05 vs. control, †CKD stage 1, ‡CKD stages 2–3, and §CKD stages 4–5.

used for statistical analyses. Values of $P <$ 0.05 were considered statistically significant.

RESULTS

Comparison of baseline clinical variables among groups according to CKD stage

Baseline demographic and clinical characteristics, laboratory values, and history of medication for participants are reported in Table 1. Duration of diabetes, serum creatinine, eGFR$_{MDRD}$, and urinary albumin-to-creatinine ratio levels were significantly higher in the CKD groups than in the control, and increased with increasing CKD stage. There were significant differences in 1,5-AG and FPG levels but no significant difference in HbA$_{1c}$ levels among groups.

Correlations among 1,5-AG, eGFR$_{MDRD}$, and other clinical variables

The ln(1,5-AG) values were significantly negatively correlated with FPG and HbA$_{1c}$ levels, except for CKD stages 4–5. However, 1,5-AG was not associated with serum creatinine or eGFR$_{MDRD}$ in a simple correlation analysis (Supplementary Table S1). Analysis of stepwise multivariate regression is reported in Table 2. For the control group and CKD stages 1–3, HbA$_{1c}$ was a consistently explanatory variable of 1,5-AG. FPG, age, duration of diabetes, and medication of antihypertension were significantly associated with 1,5-AG (all $P < 0.001$,

irrespective of groups and models). However, eGFR$_{MDRD}$ was the only independent determinant of 1,5-AG levels for CKD stages 4–5.

Correlations between ln(1,5-AG) and HbA$_{1c}$ or FPG levels according to CKD stages

Figure 1 illustrates that the inverse correlations between ln(1,5-AG) and HbA$_{1c}$ levels remain significant in the control ($R^2 = 0.534$), CKD stages 1–2 ($R^2 = 0.481$), and CKD stage 3 ($R^2 = -0.483$) groups (all $P < 0.001$), but not for the CKD stages 4–5 group ($R^2 = 0.057$, $P = 0.274$; Fig. 1). Similarly, ln(1,5-AG) is inversely correlated with FPG in the control ($R^2 = 0.414$), CKD stages 1–2 ($R^2 = 0.356$) and CKD stage 3 groups ($R^2 = 0.227$, all $P < 0.001$), but not for the CKD stages 4–5 group ($R^2 = 0.145$, $P = 0.080$; Fig. 2).

CONCLUSIONS

Although 1,5-AG appears to be more useful than HbA$_{1c}$ as a short-term marker of glycemic control and more specific in the assessment of postprandial hyperglycemia for subjects with well or moderately controlled diabetes (15,17,18), it has limitations for use in subjects with renal tubular acidosis, uremia, or end-stage renal disease (ESRD). However, the relationship between 1,5-AG levels and mild or moderate renal dysfunction, which is the most common stage of CKD in subjects with type 2 diabetes, is unclear.

The current study detected no relationships between 1,5-AG values and

eGFR$_{MDRD}$ for CKD stages 1–3 in a relatively large sample of Korean subjects with type 2 diabetes. Moreover, the associations between 1,5-AG and HbA$_{1c}$ or FPG levels were strongly significant in subjects with CKD stages 1–3, but not in subjects with CKD stages 4–5. This suggests that 1,5-AG levels reflect glycemic state and might be useful for assessing glycemic control if patients are in a state of mild or moderate renal dysfunction.

This study showed that eGFRs have influence on 1,5-AG levels not in subjects with mild or moderate renal dysfunction but in those with severe renal dysfunction or ESRD. Possible contributions of renal tubular damage to serum (or plasma) 1,5-AG levels have been shown in several case–control reports. Some reports have claimed that 1,5-AG levels are not valid for subjects with uremia or chronic renal failure; 1,5-AG levels in these groups were as low as those in a type 2 diabetes group, significantly lower than those in healthy controls (19,20), and negatively correlated with serum creatinine (21). However, the numbers of study participants in these studies were small ($n = 32–75$). On the other hand, a study by Yamanouchi et al. (22) showed that renal dysfunction has little influence on 1,5-AG concentrations. These inconsistent results might be due to group or classification discrepancies. This study was the first to analyze 1,5-AG concentrations in type 2 diabetes classified by CKD stage.

Table 2—*Stepwise multivariate linear regression analyses as independent determinants of ln(1,5-AG) according to CKD stages*

| | Ln(1,5-AG) | | | | | | | |
| | Control | | CKD stages 1–2 | | CKD stage 3 | | CKD stages 4–5 | |
	β	P	β	P	β	P	β	P
Model 1								
HbA$_{1c}$	−0.741	<0.001	−0.694	<0.001	−0.695	<0.001		
Model 2								
HbA$_{1c}$	−0.368	0.009	−0.563	<0.001	−0.702	<0.001		
FPG	−0.466	0.001	−0.217	0.022				
Age			0.139	0.049				
eGFR$_{MDRD}$							0.720	0.013
Model 3								
HbA$_{1c}$	−0.321	0.019	−0.495	<0.001	−0.603	<0.001		
FPG	−0.538	<0.001	−0.254	0.008				
Duration of diabetes					−0.233	0.019		
eGFR$_{MDRD}$							0.907	0.012
Antihypertension medication			0.189	0.009				

Covariables that are not significant in the models are deleted in the Table. Model 1: age, sex, HbA$_{1c}$, duration of diabetes, and eGFR$_{MDRD}$. Model 2: Model 1 plus FPG, systolic blood pressure, HDL, and triglycerides. Model 3: Model 2 plus smoking status and use of antihypertension and antidyslipidemia medication.
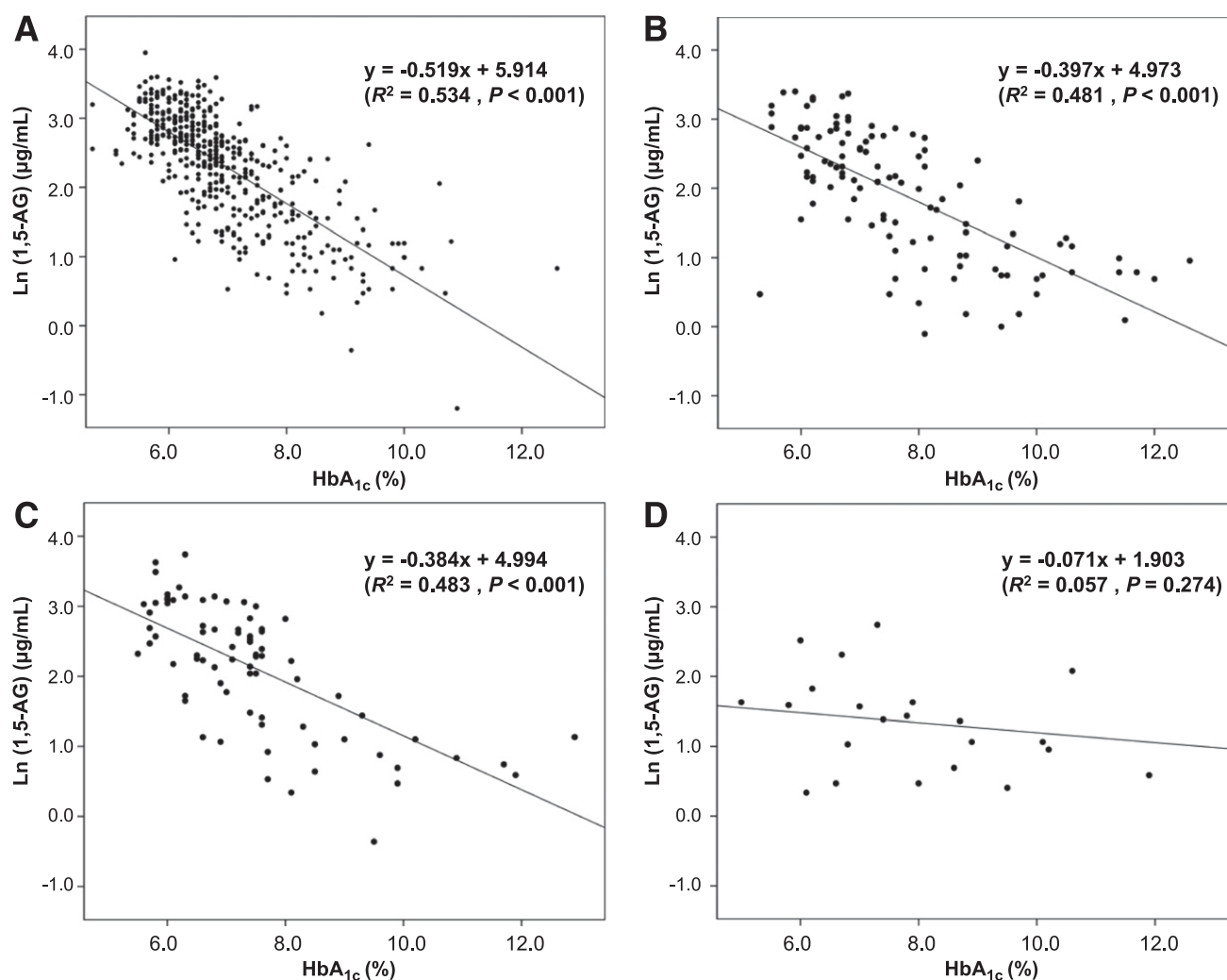
Figure 1—*Simple linear regression analyses demonstrated that 1,5-AG levels had significantly inverse correlations with HbA_{1c} levels in normal renal function* (A), *in CKD stages 1–2* (B) *and 3* (C), *but not in CKD stages 4–5* (D).

Although some have suggested that 1,5-AG levels cannot be used as a reliable index of glycemic control when subjects are in a state of renal dysfunction (14,20,23), 1,5-AG levels in this study had significant inverse correlations with HbA_{1c} and FPG levels when subjects had normal to moderate renal dysfunction. However, caution should be taken when using 1,5-AG values as markers of glycemic control in cases of severe renal dysfunction or ESRD. Although little information is available regarding the contribution of renal impairment to the tubular reabsorption of 1,5-AG through sodium glucose cotransporter 4 (SGLT4), a recently described candidate transporter of 1,5-AG (24,25), it may be conferred from the studies of other glucose transporters. For nephrectomized rats, expression, but not activity, of glucose transporters decreased (26), and glucose transporters in brush-border membranes

diminished in spontaneous idiopathic Fanconi syndrome (27). As CKD stage or renal tubular damage progresses, it is possible that resorption of 1,5-AG would be reduced due to a decrease in SGLT4s and aggravated damage of glucose cotransporters. Until now, there were no actual data to support this hypothesis. Further understanding of the characteristics of SGLTs under renal dysfunction is needed.

FPG and 1,5-AG are correlated ($r = -0.381$, $P = 0.080$), and this relationship is stronger than the correlation between 1,5-AG and HbA_{1c} ($r = -0.238$, $P = 0.274$) in subjects with CKD stages 4–5. Emoto et al. (14) revealed that inverse correlations between 1,5-AG and HbA_{1c} or FPG in diabetic patients with normal renal function were not present in patients with ESRD. However, most patients with ESRD underwent dialysis, which is known to affect 1,5-AG levels. HbA_{1c} measurements in

subjects with an aggravated CKD state could be unreliable and confounded by other factors, including shortened erythrocyte life span, blood transfusion, and accelerated erythropoiesis because of anemia and use of erythropoietin. Although it is possible that the association between 1,5-AG and HbA_{1c} could be insignificant in the CKD stages 4–5 group, the correlation between 1,5-AG and FPG should explored in future studies with a large sample size.

The main strengths of the present work are the relatively large study sample and the careful characterization of the participants, during which the relationships between 1,5-AG levels and $eGFR_{MDRD}$ or CKD stages were first evaluated. The limitations of this study are that subjects self-reported their medical history and subjects with renal tubular acidosis were included, which may have confounded the results. In addition, the number of participants with CKD
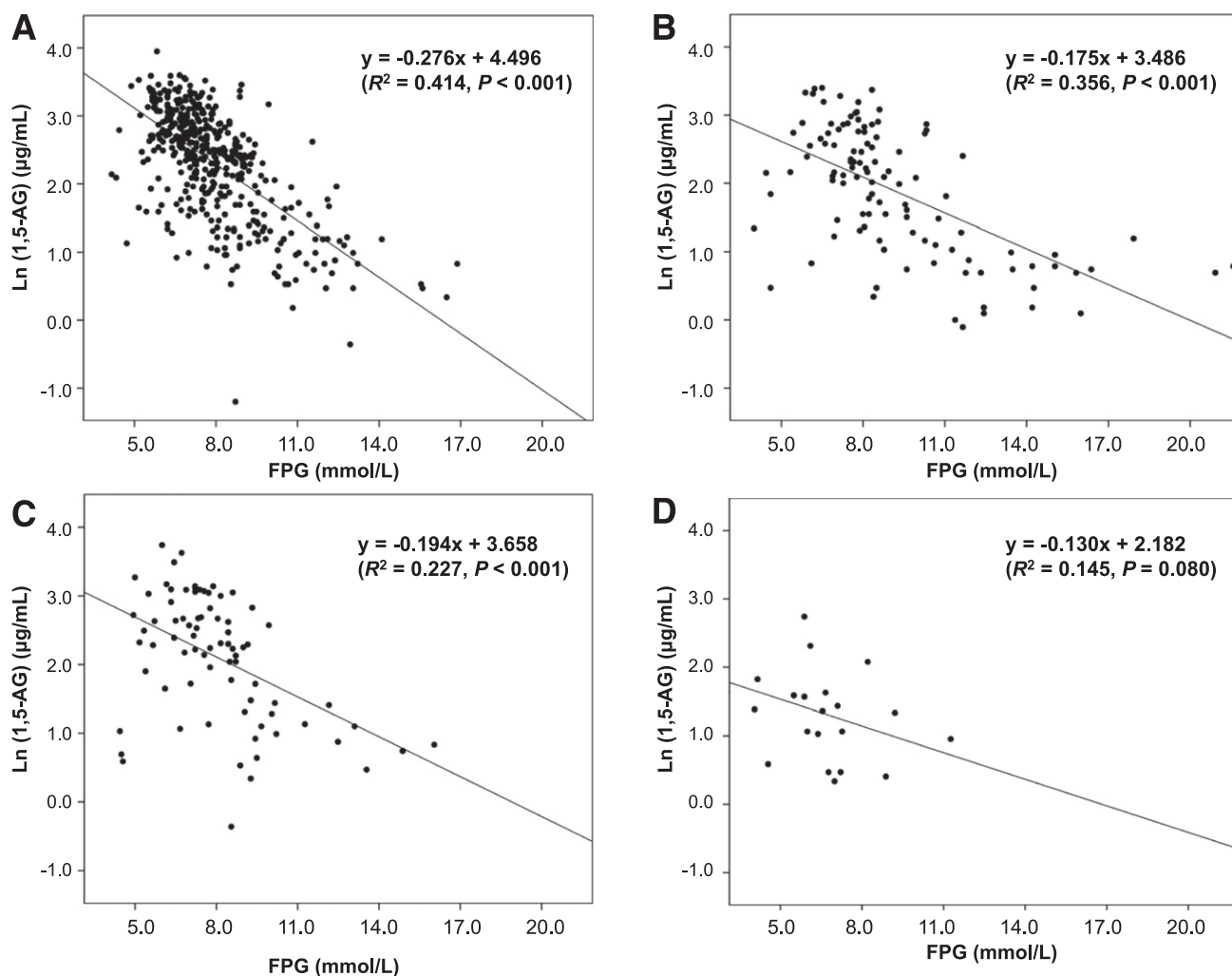
Figure 2—*Simple linear regression analyses demonstrated that 1,5-AG levels had significantly inverse correlations with FPG levels in normal renal function* (A)*, in CKD stages 1–2* (B) *and 3* (C)*, but not in CKD stages 4–5* (D)*.*

stages 4–5 was small. A sophisticated study of a large number of subjects with severe renal impairment or ESRD would help improve the understanding of the effects of renal impairment on 1,5-AG levels.

In conclusion, this study demonstrated that mild or moderate renal dysfunction appears to have no effect on serum 1,5-AG concentrations and that the relationship between 1,5-AG and glycemic markers suggests that 1,5-AG levels may be useful for monitoring glycemic control in subjects with CKD stages 1–3.

References
1. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med 2008;358:580–591
2. Hovind P, Rossing P, Tarnow L, Smidt UM, Parving HH. Progression of diabetic nephropathy. Kidney Int 2001;59:702–709
3. Gilbert RE, Tsalamandris C, Bach LA, et al. Long-term glycemic control and the rate of progression of early diabetic kidney disease. Kidney Int 1993;44:855–859
4. Hasslacher C, Bostedt-Kiesel A, Kempe HP, Wahl P. Effect of metabolic factors and blood pressure on kidney function in proteinuric type 2 (non-insulin-dependent) diabetic patients. Diabetologia 1993;36:1051–1056
5. Yamanouchi T, Ogata N, Tagaya T, et al. Clinical usefulness of serum 1,5-anhydroglucitol in monitoring glycaemic control. Lancet 1996;347:1514–1518
6. Dungan KM, Buse JB, Largay J, et al. 1,5-anhydroglucitol and postprandial hyperglycemia as measured by continuous glucose monitoring system in moderately controlled patients with diabetes. Diabetes Care 2006;29:1214–1219
7. Dungan KM. 1,5-anhydroglucitol (GlycoMark) as a marker of short-term glycemic control and glycemic excursions. Expert Rev Mol Diagn 2008;8:9–19
8. Akanuma Y, Morita M, Fukuzawa N, Yamanouchi T, Akanuma H. Urinary excretion of 1,5-anhydro-D-glucitol accompanying glucose excretion in diabetic patients. Diabetologia 1988;31:831–835
9. Yamanouchi T, Minoda S, Yabuuchi M, et al. Plasma 1,5-anhydro-D-glucitol as new clinical marker of glycemic control in NIDDM patients. Diabetes 1989;38:723–729
10. Yamanouchi T, Akanuma Y, Toyota T, et al. Comparison of 1,5-anhydroglucitol,

HbA1c, and fructosamine for detection of diabetes mellitus. Diabetes 1991;40:52–57

11. Tam WH, Rogers MS, Lau TK, Arumanayagam M. The predictive value of serum 1,5-anhydro-D-glucitol in pregnancies at increased risk of gestational diabetes mellitus and gestational impaired glucose tolerance. BJOG 2001;108:754–756

12. Kilpatrick ES, Keevilt BG, Richmond KL, Newland P, Addison GM. Plasma 1,5-anhydroglucitol concentrations are influenced by variations in the renal threshold for glucose. Diabet Med 1999;16:496–499

13. Fujisawa T, Ikegami H, Tsutsui T, et al. Renal tubular function affects glycosuria-related urinary excretion of 1,5-anhydroglucitol. Diabetes Care 1999;22:863–864

14. Emoto M, Tabata T, Inoue T, Nishizawa Y, Morii H. Plasma 1,5-anhydroglucitol concentration in patients with end-stage renal disease with and without diabetes mellitus. Nephron 1992;61:181–186

15. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39(Suppl. 1):S1–S266

16. Won JC, Park CY, Park HS, et al. 1,5-Anhydroglucitol reflects postprandial hyperglycemia and a decreased insulinogenic index, even in subjects with prediabetes and well-controlled type 2 diabetes. Diabetes Res Clin Pract 2009; 84:51–57

17. Kishimoto M, Yamasaki Y, Kubota M, et al. 1,5-Anhydro-D-glucitol evaluates daily glycemic excursions in well-controlled NIDDM. Diabetes Care 1995;18:1156–1159

18. Stettler C, Stahl M, Allemann S, et al. Association of 1,5-anhydroglucitol and 2-h postprandial blood glucose in type 2 diabetic patients. Diabetes Care 2008;31: 1534–1535

19. Shimizu H, Shouzu A, Nishikawa M, et al. Serum concentration and renal handling of 1,5-anhydro-D-glucitol in patients with chronic renal failure. Ann Clin Biochem 1999;36:749–754

20. Niwa T, Dewald L, Sone J, Miyazaki T, Kajita M. Quantification of serum 1,5-anhydroglucitol in uremic and diabetic patients by liquid chromatography/mass spectrometry. Clin Chem 1994;40:260–264

21. Yamada H, Hishida A, Kato A, Yoneyama T. 1,5-anhydroglucitol as a marker for the differential diagnosis of acute and chronic renal failure. Nephron 1996;73:707–709

22. Yamanouchi T, Akanuma H, Nakamura T, Akaoka I, Akanuma Y. Reduction of plasma 1,5-anhydroglucitol (1-deoxyglucose) concentration in diabetic patients. Diabetologia 1988;31:41–45

23. Ichikawa H, Nagake Y, Takahashi M, et al. What is the best index of glycemic control in patients with diabetes mellitus on hemodialysis? Nippon Jinzo Gakkai Shi 1996;38:305–308

24. Yamanouchi T, Shinohara T, Ogata N, Tachibana Y, Akaoka I, Miyashita H. Common reabsorption system of 1,5-anhydro-D-glucitol, fructose, and mannose in rat renal tubule. Biochim Biophys Acta 1996;1291:89–95

25. Tazawa S, Yamato T, Fujikura H, et al. SLC5A9/SGLT4, a new Na+-dependent glucose transporter, is an essential transporter for mannose, 1,5-anhydro-D-glucitol, and fructose. Life Sci 2005;76:1039–1050

26. Nakamura N, Masuda S, Takahashi K, Saito H, Okuda M, Inui K. Decreased expression of glucose and peptide transporters in rat remnant kidney. Drug Metab Pharmacokinet 2004;19:41–47

27. Medow MS, Reynolds R, Bovee KC, Segal S. Proline and glucose transport by renal membranes from dogs with spontaneous idiopathic Fanconi syndrome. Proc Natl Acad Sci USA 1981;78:7769–7772