Journal of Diabetes and Its Complications 30 (2016) 786–789

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Serum albumin-adjusted glycated albumin is a better predictor of mortality in diabetic patients with end-stage renal disease on hemodialysis

Takahiro Yajima [a,*], Kumiko Yajima [b], Makoto Hayashi [b], Keigo Yasuda [b], Hiroshi Takahashi [c], Noriyoshi Yamakita [b]

[a] Department of Nephrology, Matsunami General Hospital, Gifu 501-6062, Japan
[b] Department of Internal Medicine, Matsunami General Hospital, Gifu 501-6062, Japan
[c] Division of Medical Statistics, Fujita Health University School of Medicine, Aichi 470-1192, Japan

ARTICLE INFO

Article history:
Received 13 January 2016
Received in revised form 25 February 2016
Accepted 29 February 2016
Available online 2 March 2016

Keywords:
GA
Adjusted GA
Type 2 diabetes
ESRD
Hemodialysis

ABSTRACT

Aims: Glycated albumin (GA) is a marker for monitoring glycemic control in diabetic patients with end-stage renal disease (ESRD). We evaluated whether serum albumin-adjusted GA (adjusted GA) could predict mortality in diabetic patients with ESRD on hemodialysis.
Methods: Seventy-eight patients with type 2 diabetes treated with regular hemodialysis were enrolled and followed up for 5-years. The adjusted GA was calculated from the regression formula and mean GA. The cut-off values for GA and adjusted GA that predicted mortality risk were determined using receiver operating characteristic curve analysis.
Results: During the follow-up period (median: 36 months), 15 patients died. In the Kaplan–Meier analysis, there were no significant differences in the 5-year cumulative survival rate (58.3% [GA ≥19.8%] vs. 88.6% [GA <19.8%], $P = 0.075$). Conversely, this rate was significantly higher in patients with adjusted GA <21.2% than adjusted GA ≥21.2% (86.4 vs. 49.5%, $P = 0.0068$). After adjustment for other confounders, adjusted GA ≥21.2% was an independent predictor for mortality (hazard ratio 3.76, 95% confidence interval 1.12–17.44, $P = 0.031$), but GA ≥19.8% was not (hazard ratio 2.63, 95% confidence interval 0.65–17.69, $P = 0.19$).
Conclusions: Adjusted GA is a better predictor of mortality than GA in diabetic patients with ESRD on hemodialysis.

1. Introduction

In diabetic patients, glycemic control is important for the prevention of microvascular and macrovascular complications (The Diabetes Control & Complications Trial Research Group, 1993; UK Prospective Diabetes Study (UKPDS) Group (1998); Gaede et al., 2003). Although HbA1c has been widely used as a standard marker for glycemic control, it underestimates glycemic control in diabetic patients with end-stage renal disease (ESRD) on hemodialysis due to the shortened lifespan of red cells, blood loss, or bleeding during hemodialysis therapy and the administration of erythropoiesis-stimulating agents (Ansari, Thomas, & Goldsmith, 2003; Nakao et al., 1998). In contrast, glycated albumin (GA), which is not influenced by erythrocyte lifespan or erythropoietin therapy, may more accurately reflect the glycemic control during the preceding 2–3 weeks (Chujo et al., 2006; Inaba et al., 2007; Peacock et al., 2008). Therefore, GA may be an alternative marker for glycemic control in diabetic ESRD patients on hemodialysis. Some observational studies showed that a higher GA level was a significant predictor of mortality in diabetic patients with ESRD compared to a lower GA level (Fukuoka et al., 2008; Isshiki et al., 2014).

Recently, serum albumin-adjusted glycated albumin has been reported to be a better indicator of glycemic control in diabetic patients with ESRD who are not on hemodialysis (Fukami et al., 2015a, 2015b), but its impact on long-term survival in diabetic patients with ESRD is unknown. In this study, we investigated whether adjusted GA could more accurately predict mortality in diabetic patients with ESRD on hemodialysis.

2. Patients and methods

This prospective observational study was designed to assess the associations between glycemic control and patient survival.

Conflicts of interest: none.

* Corresponding author at: Department of Nephrology, Matsunami General Hospital, 185-1, Dendai, Kasamatsu, Gifu, 501-6062, Japan. Tel.: +81 58 388 0111; fax: +81 58 388 4711.
E-mail address: yajima5639@gmail.com (T. Yajima).

http://dx.doi.org/10.1016/j.jdiacomp.2016.02.021
1056-8727/

2.1. Patients

Seventy-eight patients with type 2 diabetes who had undergone maintenance hemodialysis for >1 month at our outpatient clinic were enrolled. The diagnosis of type 2 diabetes mellitus was based on history and on the diagnostic and classification criteria for diabetes mellitus (American Diabetes Association, 2010). Patients with type 1 diabetes were excluded. All patients underwent regular hemodialysis three times a week with a high-flux membrane and standard bicarbonate dialysate.

2.2. Clinical and laboratory parameters

The patients underwent routine clinical examinations before their regular hemodialysis sessions. The blood samples for the laboratory tests were drawn with the patient in a supine position before the start of the hemodialysis session on a Monday or Tuesday. GA was measured using an enzymatic method and a liquid chemistry system (GA assay; Asahi Kasei, Tokyo, Japan) on a clinical auto-analyzer. The reference range for GA was between 11 and 16%. To calculate baseline GA and serum albumin, they were measured monthly for 3 months before the observation, and the average values of three values was used as the baseline value.

2.3. Observational study

This observational portion of the study was performed from October 2010 to November 2015, and the patient survival was monitored until November 2015. The primary endpoint was all-cause mortality. This study was approved by the ethics committee of our hospital (No. 294), and all patients gave informed consent to participate in this study.

2.4. Statistical analysis

Normally distributed variables were expressed as mean ± standard deviation (SD) and non-normally distributed variables as median and interquartile range (IQR). The regression analysis between the measured GA and serum albumin levels was performed; subsequently, the adjusted GA levels were calculated using the regression formula and the mean value of the measured GA. A receiver operating characteristic (ROC) curve for GA and adjusted GA was constructed to identify the optimum cut-off values for the prediction of mortality. The differences in event-free survival between the two groups were examined with the Kaplan–Meier method and compared using a log-rank test. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated for each endpoint by a Cox proportional hazards analysis. The multivariate regression model included the covariates that had a P value of <0.1 on the univariate analysis. All statistical analyses were performed using the SPSS 21 software program (SPSS Inc., Chicago, IL, USA). P values of <0.05 were considered statistically significant.

3. Results

3.1. Clinical and laboratory characteristics at baseline

The patients' baseline characteristics are summarized in Table 1. The mean or median values were as follows: duration of hemodialysis, 20 months; Alb, 36 g/L; and GA, 21.1%. At baseline, 44 of the 78 (56%) patients had history of cardiovascular disease (CVD), including chronic heart failure ($n = 28$), coronary artery disease ($n = 25$), and cerebrovascular disease ($n = 8$). The participants used the following diabetes therapies: diet ($n = 11$), oral hypoglycemic agents ($n = 15$), and insulin ($n = 52$) (Table 1).

Table 1
Patient characteristics.

	$N = 78$
Age (years)	65 ± 11
Male/female (n)	58/20
Duration of hemodialysis (months)	20 (1.2–76)[a]
Body mass index (kg/m^2)	23 ± 3
History of hypertension (n)	77
History of smoking (n)	14
History of cardiovascular diseases (n)	44
Therapy for diabetes (n)	Diet ($n = 11$), oral hypoglycemic agents ($n = 15$), insulin ($n = 52$)
Hemoglobin (g/L)	101 ± 12
Serum albumin (g/L)	36 ± 3
Uric acid (μmol/L)	428 ± 83
C-reactive protein (μg/L)	1800 (900–3800)[a]
BUN (mmol/L)	19 ± 5
Cre (μmol/L)	742 ± 282
Total cholesterol (mmol/L)	4.0 ± 0.9
LDL-C (mmol/L)	2.3 ± 0.7
HDL-C (mmol/L)	1.1 ± 0.3
TG (mmol/L)	1.5 ± 0.9
Serum calcium (mmol/L)	2.2 ± 0.2
Serum phosphorus (mmol/L)	1.5 ± 0.5
Ferritin (ng/mL)	109 (57–179)[a]
Intact PTH (pg/mL)	133 (82–215)[a]
Blood glucose (mmol/L)	9.1 ± 3.4
HbA1c (%)	6.2 ± 0.8
Glycated albumin (%)	21.1 ± 4.3
Kt/V urea	1.1 ± 0.3
Normalized protein catabolic rate (g/kg/day)	0.93 ± 0.18
Erythropoietin dose (U/week)	6559 ± 5009

Values are mean ± standard deviation unless otherwise indicated.
[a] Median (IQR) values.

3.2. Correlation between glycated albumin (GA) and serum albumin levels

GA was positively correlated with the serum albumin levels ($r = 0.275$, $P = 0.015$, Fig. 1). Adjusted GA was calculated using the regression formula (GA [%] = 0.298 × Alb [g/L] + 10.1) and the mean value of the measured GA (21.1%) referring to the concept of formula reported by Fukami et al. (2015a).

$$\text{adjusted GA}(\%) = \text{GA}(\%) \times 21.1/(0.298 \times \text{Alb}[\text{g/L}] + 10.1).$$

3.3. Follow-up study

During the follow-up period (median, 36 months), 15 (19%) of the study participants died (three without a history of CVD and 12 with a history of CVD) due to infectious diseases ($n = 1$ and 4, respectively), CVD ($n = 1$ and 3, respectively), malignancy ($n = 1$ and 2, respectively), or other causes ($n = 0$ and 3, respectively).

The HRs for GA and adjusted GA for mortality were 1.09 (95% CI 0.98–1.20, $P = 0.11$) and 1.10 (95% CI 0.99–1.23, $P = 0.065$), respectively. The HRs for GA and adjusted GA for mortality was 1.09 (95% CI 0.96–1.23, $P = 0.17$) and 1.09 (95% CI 0.96–1.23, $P = 0.16$) after adjustment for sex, and age, history of CVD, and insulin therapy, which were covariates with a P value of <0.1 by univariate analysis (Table 2). The areas under the ROC curves for GA and adjusted GA were 0.730 ($P = 0.0073$) and 0.733 ($P = 0.0059$) respectively, and the cut-off values for predicting mortality risk were 19.8 and 21.2%, respectively. The HR of GA ≥ 19.8% for mortality was 3.54 (95% CI 0.97–22.71, $P = 0.055$) and was 2.63 (95% CI 0.65–17.69, $P = 0.19$) after adjustment. In contrast, the HR of adjusted GA ≥21.2% for mortality was 4.85 (95% CI 1.54–21.33, $P = 0.005$) and was 3.76 (95% CI 1.12–