Baseline aspartate aminotransferase/alanine transaminase ratio is associated with 3-year mortality in peritoneal dialysis patients

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To the Editor: Peritoneal dialysis (PD) is a well-established renal replacement therapy in end-stage renal disease (ESRD) patients. Despite significant advances in technologies in recent decades, the mortality of PD patients remains high. Identifying prognostic factors for PD patients may help to identify patients at high risk. The aspartate aminotransferase (AST)/alanine transaminase (ALT) ratio was originally proposed as a marker of hepatic diseases. In recent years, researchers have found this ratio to be related to morbidity and mortality in other populations as well.[1,2] Therefore, we conducted this study to evaluate the prognostic value of the aspartate aminotransferase/alanine transaminase ratio (AST/ALT) ratio in PD patients.

This prospective cohort study was performed at West China Hospital, Sichuan University. Patients were included if they started PD treatment at our center and agreed to receive follow-up. Patients were excluded if they were <18 years old or had active hepatitis or cirrhosis. Patients who were admitted at our institution for PD treatment between January 1, 2011 and October 31, 2017 were recruited to participated in this study. Subjects included were followed until their death or October 31, 2020, whichever occurred first. Follow-up was conducted by phone interviews and through medical records. The patients who underwent kidney transplant or were transferred to hemodialysis were censored at the time of transfer to alternative renal replacement therapy. The major outcome was 3-year mortality. All participants provided informed consent, and the study was approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University (No. 2019793).

Data on demographics, the underlying cause of ESRD, morbidities, and medications were collected at baseline. Fasting venous blood samples were collected before PD initiation and sent to the Laboratory Center of West China Hospital for laboratory parameter measurements (including serum hemoglobin, albumin, magnesium, urea, calcium, phosphate, high-density lipoprotein cholesterol, AST, and ALT). PD-related parameters were collected within 3 months of PD initiation. Total removal of waste products was measured as clearance estimated by total weekly Kt/V urea (/week) and total weekly creatinine clearance ($L \cdot week^{-1} \cdot 1.73\ m^{-2}$). A 24-h urine collection was used to calculate the residual glomerular filtration rate (GFR). A standard peritoneal equilibration test was performed, and the dialysate-to-plasma (D/P) creatinine concentration ratio at 4 h of the dwell was used to classify peritoneal membrane transport status. Patients were categorized as slow (4-h D/P creatinine <0.50), average (4-h D/P creatinine between 0.50 and 0.81), and fast transporters (4-h D/P creatinine >0.81).[3]

Continuous variables are summarized as the mean ± standard deviation or median with interquartile ranges. Categorical variables are expressed as percentages. We used the chi-squared test for comparing proportions and the two-sample *t* test or Wilcoxon rank-sum test for comparing continuous variables as appropriate. Survival curves were generated by the Kaplan-Meier method and compared using the log-rank test. Factors predictive of all-cause mortality were identified with univariate and multivariable Cox proportional hazards regression models. Competing risk analysis was also performed with transfer to hemodialysis and renal transplantation as competing events. The level of significance was set at 0.05. All analyses were performed using Stata 11.0 (StataCorp. 2011, TX: StataCorp LP, Lakeway Drive College Station, USA).

Among 861 patients who started PD at our center, a total of 831 patients completed the 3-year follow-up. Thirty patients (3%) were lost to follow-up due to transfer to other PD centers and loss of contact. During the follow-up, 78 patients died (9.4%), 98 patients received renal transplantation (11.8%), and 93 patients were transferred to hemodialysis (11.2%). Six-month, 1- and 3-year mortality rates were 1.1%, 2.0%, and 9.4%, respectively.

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The baseline characteristics of these patients are shown in [Supplementary Table 1, http://links.lww.com/CM9/B57]. The mean age was 52.2 ± 14.4 years, and 60.2% were male. The three leading causes of ESRD were chronic glomerulonephritis (64.9%), diabetes mellitus (13.9%), and hypertension (12.9%). The median Kt/V urea week was 1.98. There were 103 fast transporters (12.4%) and 52 slow transporters (6.3%). The median AST/ALT value was 1.16 (interquartile range 0.86–1.56).

We first performed univariate Cox regression analysis using baseline characteristics, which revealed prognostic factors for 3-year mortality, including old age, high diastolic blood pressure, diabetes, cardiovascular disease, respiratory disease, low albumin, high AST/ALT ratio, low serum magnesium, low weekly Kt/V urea, low creatinine clearance, high transport status, and low residual GFR. These results were applied to the multivariate analysis.

We then performed univariate survival analysis using AST/ALT levels as both a categorical and a continuous variable. On dividing the patients into high and low AST/ALT groups according to the median value (1.16), Kaplan–Meier survival curves showed that the high AST/ALT group had higher 3-year mortality rates than the low AST/ALT group (log-rank $P = 0.003$; Figure 1A). There was also a significant association between AST/ALT levels and 3-year mortality using AST/ALT as a continuous variable in the unadjusted Cox regression model (hazard ratio [HR] = 1.37, 95% confidence interval [95% CI]: 1.22–1.54). Competing risk analysis also showed AST/ALT to be a significant prognostic factor (subhazard ratio [SHR] = 1.37, 95% CI: 1.19–1.57).

Multivariate Cox analysis with different adjusted models reached consistent results: Model 1, adjusted for age, sex, diastolic blood pressure, diabetes, cardiovascular disease, and respiratory disease; Model 2, Model 1 plus other laboratory results (hemoglobin, albumin, magnesium, calcium, and phosphate); Model 3, Model 2 plus PD-related parameters (weekly total Kt/V urea, weekly creatinine clearance, residual renal function, and peritoneal transport status). In all the models above, the high AST/ALT group showed a significantly higher risk for 3-year mortality than the low AST/ALT group. In the fully adjusted model (Model 3), only age (HR = 1.05, 95% CI: 1.03–1.07), albumin (HR = 0.94, 95% CI: 0.89–0.99), and AST/ALT (HR = 1.28, 95% CI: 1.10–1.48) were significantly associated with 3-year mortality. Moreover, we performed another multivariable analysis in competing risk analysis and obtained consistent findings: there was a significant relationship between AST/ALT and 3-year mortality (SHR = 1.26, 95% CI: 1.06–1.50 in the fully adjusted model). Restricted cubic spline regression showed a linear relationship between AST/ALT and hazard ratio for three-year mortality [Supplementary Figure 1, http://links.lww.com/CM9/B57].

In further subgroup analysis, we tested the possible association between AST/ALT and 3-year mortality in subgroups of patients stratified by age, diabetes status, and albumin levels. High AST/ALT levels were associated with increased 3-year mortality only in patients aged

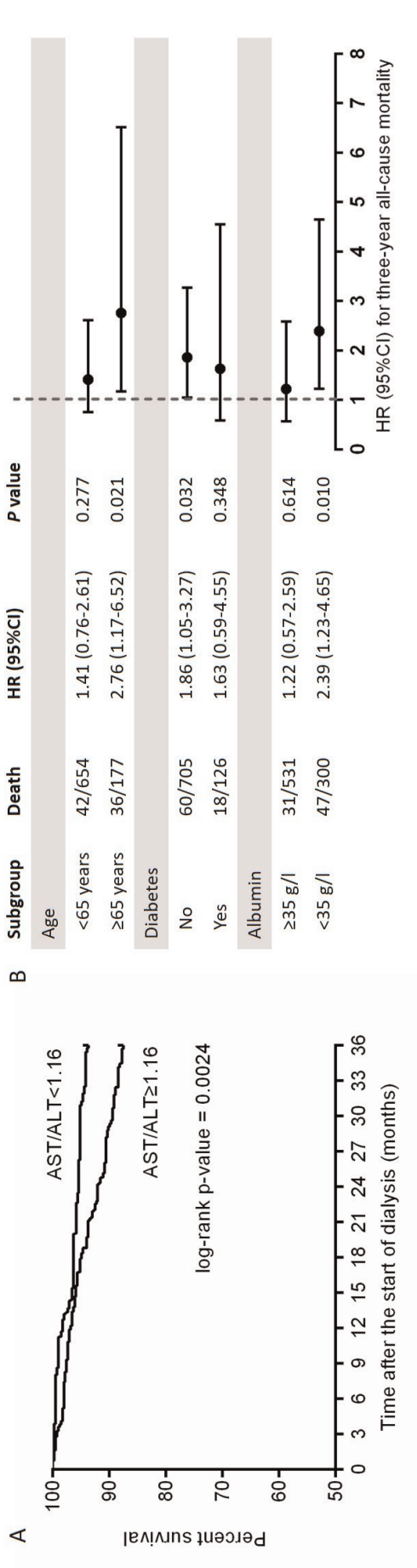

Figure 1: (A) Kaplan-Meier curve of 3-year survival according to AST/ALT group (cut-off: 1.16). (B) Subgroup analysis showing the adjusted HR for 3-year mortality In the high AST/ALT group compared with the low AST/ALT group. 95% CI: 95% confidence interval; AST/ALT: Aspartate aminotransferase/alanine transaminase ratio; HR: Hazard ratio.

>65 years, without diabetes, and with low albumin levels (<35 g/L) [Figure 1B].

To conclude, our study identified a high baseline AST/ALT ratio as a prognostic factor for 3-year mortality in PD patients. As this test is routinely performed in clinical practice, it can be used as a biomarker for risk prediction in patients who would like to choose PD as renal replacement therapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the forms, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and that due efforts will be made to conceal their identity, although anonymity cannot be guaranteed.

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Conflicts of interest

None.

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