Research Square

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Association Between Time-Varying Serum Albumin and All-Cause Mortality in Peritoneal Dialysis Patients: A Retrospective Cohort Study Time-Varying Serum Albumin and Mortality in Peritoneal Dialysis

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Abstract

Background

Serum albumin is an established prognostic marker in patients undergoing peritoneal dialysis (PD). However, single baseline measurements may not adequately capture its longitudinal variability. We investigated the association between time-varying serum albumin and all-cause mortality in patients undergoing PD.

Methods

We conducted a retrospective cohort study of adult patients who initiated PD at our institution. Serial serum albumin measurements were modeled as a time-varying covariate using the Andersen–Gill counting-process formulation of the Cox proportional hazards model. Models were adjusted for age, sex, and diabetes mellitus, with robust sandwich variance estimates clustered by patient. Restricted cubic spline analysis assessed potential nonlinearity.

Results

Among 1,801 patients with 7,102 laboratory records, 1,680 patients contributing 6,860 observations and experiencing 298 deaths were included in the final analysis. Higher time-varying serum albumin was independently associated with lower all-cause mortality (HR per 1 g/L increase, 0.864; 95% CI, 0.847–0.880; $P < 0.001$). Older age (HR, 1.040; 95% CI, 1.029–1.050; $P < 0.001$) and diabetes mellitus (HR, 1.777; 95% CI, 1.395–2.262; $P < 0.001$) were associated with higher mortality. Restricted cubic spline analysis showed a significant inverse association without evidence of nonlinearity (P-overall < 0.0001; P-nonlinear = 0.8962). The model had a Harrell C-index of 0.8176.

Conclusions

Time-varying serum albumin was independently associated with all-cause mortality in patients undergoing PD. Longitudinal albumin assessment may provide prognostic information beyond a single baseline measurement.

Trial registration

Not applicable.

Introduction

Peritoneal dialysis (PD) remains an important modality of kidney replacement therapy worldwide, providing continuous solute clearance while facilitating preservation of residual kidney function in patients with end-stage kidney disease.(1, 2) Despite advances in dialysis management, mortality among patients undergoing PD remains substantial, with cardiovascular disease and infectious complications representing major contributors to mortality among dialysis patients.(3, 4) Protein–energy wasting and malnutrition are important determinants of adverse outcomes in this population, partly through impaired immune function, muscle wasting, and reduced physiological reserve.(5) Accordingly, nutritional assessment is an integral component of PD care and is recommended by the International Society for Peritoneal Dialysis (ISPD).(6, 7)

Serum albumin is one of the most widely used biomarkers for nutritional and inflammatory risk assessment in dialysis populations. Numerous studies have demonstrated an inverse association between serum albumin concentration and mortality in both haemodialysis and PD cohorts, with hypoalbuminaemia consistently associated with adverse outcomes.(8, 9) Beyond nutritional status, serum albumin is influenced by multiple biological processes, including systemic inflammation, peritoneal protein loss, and hepatic synthetic function, and may therefore reflect broader aspects of a patient's clinical condition. (10, 11) Composite nutritional and inflammatory indices incorporating albumin or complementary inflammatory markers have further underscored the importance of multidimensional risk assessment in dialysis populations.(12, 13)

Although serum albumin has been extensively studied as a prognostic marker, many studies have relied on baseline measurements, which may not adequately capture the longitudinal variability of this dynamic biomarker. Serum albumin may change over time in response to acute illness, changes in nutritional intake, inflammatory episodes, and dialysis-related protein losses. (8, 14) Consequently, a single baseline measurement may not fully capture longitudinal changes in nutritional and inflammatory status and may introduce exposure misclassification. Previous studies in haemodialysis populations have suggested that longitudinal or time-varying assessment of serum albumin may provide additional prognostic information compared with baseline measurements.(15, 16) However, the prognostic significance of longitudinal serum albumin patterns in PD populations remains less extensively characterized, particularly when serum albumin is modelled as a time-varying exposure. (14, 17, 18) Moreover, whether the association between serum albumin and mortality is monotonic or exhibits a nonlinear pattern in patients undergoing PD remains incompletely understood.

We therefore aimed to investigate the association between time-varying serum albumin levels and all-cause mortality in patients undergoing PD using an Andersen–Gill counting-process formulation of the Cox proportional hazards model. We additionally evaluated the shape of the association between serum albumin and mortality using restricted cubic spline analysis.

Method

Study design and population

We conducted a retrospective observational cohort study of adult patients who initiated peritoneal dialysis (PD) at our institution. The study protocol was approved by the Institutional Review Board, and the requirement for informed consent was waived owing to the retrospective nature of the study and the use of anonymized clinical data. This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.(19)

Patients were identified from a clinical database containing 7,102 laboratory records from 1,801 unique individuals. Patients without a valid first laboratory or visit date (n = 37) were excluded, leaving 1,764 patients. Of these, 45 patients were further excluded because of invalid follow-up time, including zero or negative follow-up and one patient whose recorded detection date occurred after the date of death. This yielded 1,719 patients with valid follow-up data. An additional 39 patients were excluded because they could not contribute a valid risk interval required for the Andersen–Gill counting-process analysis, including patients with non-constructable longitudinal observation intervals. This resulted in a final analytic cohort of 1,680 patients, who experienced 298 all-cause deaths and contributed 6,860 observations to the fitted time-dependent Cox model. The patient selection process is illustrated in Fig. 1.

Data collection and laboratory measurements

Demographic characteristics, including age, sex, and diabetes mellitus status, were extracted from electronic medical records. Laboratory measurements, including serum albumin, C-reactive protein, hemoglobin, white blood cell count, neutrophil count, lymphocyte count, platelet count, blood urea nitrogen, serum creatinine, calcium, phosphorus, intact parathyroid hormone, and fasting glucose, were obtained from routine clinical laboratory records.

Serum albumin was measured using the bromocresol green method. C-reactive protein was measured using high-sensitivity immunoturbidimetry. Peritoneal dialysis adequacy was assessed using weekly Kt/V and creatinine clearance. Residual kidney function was estimated from 24-hour urine collections when available.

Outcome and follow-up

The primary outcome was all-cause mortality, defined as death from any cause during the follow-up period. Patients were followed from the initiation of PD until death, kidney transplantation, transfer to haemodialysis, or the last documented follow-up, whichever occurred first. Death dates were ascertained from hospital records, national death registries, or telephone contact with patients or their relatives. Patients who remained alive without experiencing the primary outcome were censored at the date of their last known contact. Patients who underwent kidney transplantation or transferred to haemodialysis were censored at the date of the corresponding transition.

Statistical analysis

Continuous variables were presented as median (interquartile range) or mean (standard deviation), according to the results of the Shapiro–Wilk test for normality. Between-group comparisons were performed using the Wilcoxon rank-sum test or Student's *t*-test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate.

Serum albumin was modelled as a time-varying covariate using the Andersen–Gill counting-process formulation of the Cox proportional hazards model.(20) Each patient contributed multiple observation intervals defined by start time (*tstart*) and stop time (*tstop*), with serum albumin updated at each measurement time point. The time-dependent Cox model was adjusted for age, sex, and diabetes mellitus. Clustered robust standard errors were estimated using patient identification as the clustering variable to account for within-patient correlation.

The dose–response relationship between serum albumin and all-cause mortality was examined using restricted cubic spline analysis with four knots placed at the 10th, 50th, 75th, and 90th percentiles (**27.7, 35.2, 38.4, and 41.0 g/L**, respectively). (21) Model discrimination was assessed using Harrell's C-index, (22) and model fit was assessed using the Akaike information criterion (AIC).(23) The proportional hazards assumption was evaluated using Schoenfeld residuals for the covariates included in the Cox model. (24)

All statistical analyses were performed using R software (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria), utilizing the *survival* and *rms* packages. Two-sided *P*-values < 0.05 were considered statistically significant.

Result

Patient selection and baseline characteristics

A total of 7,102 laboratory records from 1,801 unique patients were identified from the initial peritoneal dialysis database. After excluding 37 patients without a valid first laboratory or visit date, 1,764 patients remained. Of these, 45 patients were further excluded because of invalid follow-up time, including one patient whose recorded detection date occurred after the date of death, leaving 1,719 patients with valid follow-up data. An additional 39 patients were excluded because they could not contribute a valid risk interval required for the Andersen–Gill counting-process analysis. Among these, 9 deaths could not be assigned to valid counting-process intervals, while the remaining 30 patients had non-constructable or otherwise invalid longitudinal observation intervals. Consequently, the final analytic cohort comprised 1,680 patients, contributing 6,860 observations to the fitted time-dependent Cox model and experiencing 298 all-cause deaths. The patient selection process is illustrated in Fig. 1.

Baseline characteristics of the overall cohort (N = 1,801) are presented in Table S2 and illustrated in Fig. 2. During follow-up, 323 patients died in the overall cohort. The final time-dependent analysis

included 298 death events after exclusion of patients who could not contribute valid counting-process intervals.

Baseline characteristics narrative

Compared with survivors, patients who died were older (median age, 63.0 vs. 56.0 years; $P < 0.001$), had a higher prevalence of diabetes mellitus (42.1% vs. 23.5%; $P < 0.001$), and exhibited lower serum albumin concentrations (31.7 vs. 34.4 g/L; $P < 0.001$). Deceased patients also had higher C-reactive protein concentrations (7.0 vs. 4.8 mg/L; $P = 0.011$), higher haemoglobin levels (83.5 vs. 80.0 g/L; $P = 0.019$), lower blood urea nitrogen concentrations (19.2 vs. 23.4 mmol/L; $P < 0.001$), lower serum creatinine levels (677.0 vs. 779.0 μmol/L; $P < 0.001$), lower serum phosphorus concentrations (1.5 vs. 1.7 mmol/L; $P < 0.001$), lower intact parathyroid hormone levels (243.9 vs. 344.0 pg/mL; $P < 0.001$), and lower prognostic nutritional index values (37.7 vs. 40.1; $P < 0.001$).

No significant differences were observed between survivors and deceased patients regarding sex distribution (57.3% vs. 57.0%; $P = 0.969$), serum calcium concentration (2.0 mmol/L in both groups; $P = 0.750$), white blood cell count (6.9 vs. 6.7 $\times 10^9$/L; $P = 0.539$), platelet count (204.5 vs. 205.0 $\times 10^9$/L; $P = 0.852$), neutrophil-to-lymphocyte ratio (4.3 vs. 4.2; $P = 0.772$), or lymphocyte count (1.1 $\times 10^9$/L in both groups; $P = 0.507$).

Univariable Cox proportional hazards analysis

Univariable Cox proportional hazards analyses were performed using a complete-case cohort of 1,094 patients, among whom 159 deaths occurred (Table S3). Patients with missing information for one or more variables included in the analysis were excluded from this specific analysis.

Time-dependent Cox proportional hazards model

The time-dependent Cox proportional hazards model was fitted among 1,680 patients contributing 6,860 observations and 298 death events. Serum albumin, incorporated as a time-varying covariate, was independently associated with all-cause mortality (HR per 1 g/L increase, 0.864; 95% CI, 0.847–0.880; $P < 0.001$) (Table S3).

Each 1 g/L increase in time-varying serum albumin was associated with an approximately 13.6% lower hazard of death. Older age remained independently associated with increased mortality risk (HR, 1.040; 95% CI, 1.029–1.050; $P < 0.001$), and diabetes mellitus was also associated with higher mortality risk (HR, 1.777; 95% CI, 1.395–2.262; $P < 0.001$). Male sex was not significantly associated with mortality in the adjusted time-dependent model (HR, 1.065; 95% CI, 0.843–1.344; $P = 0.598$) (Fig. 3).

The time-dependent Cox model demonstrated good discrimination, with a Harrell's C-index of 0.8176. Model fit was assessed using the Akaike information criterion (AIC = 3487.22). The proportional hazards

assumption was evaluated using Schoenfeld residuals, with detailed results provided in Supplementary Table S3.

Dose–response relationship between serum albumin and mortality

Restricted cubic spline analysis was performed to characterize the dose–response relationship between serum albumin and all-cause mortality risk (Fig. 4). Across the observed serum albumin range of 11.4–59.4 g/L, higher albumin concentrations were consistently associated with lower mortality hazard.

The overall association was statistically significant (*P*-overall < 0.0001). The test for nonlinearity was not significant (*P*-nonlinear = 0.8962), indicating no evidence of a nonlinear association within the observed range. The association therefore appeared predominantly monotonic and inverse, with no evidence of a J-shaped or U-shaped pattern.

Survival analysis according to baseline serum albumin quartiles

Kaplan–Meier survival curves stratified according to baseline serum albumin quartiles are presented in Fig. 5. Patients were categorized into four groups according to the baseline serum albumin distribution: Q1 (≤ 30.0 g/L), Q2 (> 30.0–33.8 g/L), Q3 (> 33.8–37.6 g/L), and Q4 (> 37.6 g/L).

Survival probability increased progressively across increasing baseline serum albumin quartiles, with clear separation of the survival curves during follow-up. The log-rank test demonstrated significant differences in survival among the four groups (*P* < 0.001). At 120 months of follow-up, survival probability was lowest among patients in Q1 and highest among those in Q4.

Discussion

Repeatedly measured serum albumin was independently associated with all-cause mortality in patients undergoing peritoneal dialysis, with each 1 g/L increase in time-varying serum albumin associated with a 13.6% lower hazard of death. The time-dependent Cox model incorporating serum albumin, age, sex, and diabetes mellitus included 1,680 patients, who contributed 6,860 observations and experienced 298 deaths, and demonstrated good discrimination, with a C-index of 0.8176. Restricted cubic spline analysis demonstrated a monotonic inverse dose–response relationship between serum albumin and mortality risk across the observed range (11.4–59.4 g/L), with no evidence of statistical nonlinearity (*P*-overall < 0.0001; *P*-nonlinear = 0.8962). These findings suggest that time-varying serum albumin may serve as a clinically relevant longitudinal marker reflecting the evolving nutritional and inflammatory status of patients undergoing peritoneal dialysis.

The association between lower serum albumin and increased mortality in patients undergoing PD likely reflects multiple interconnected biological pathways. Serum albumin is influenced by multiple biological processes, including nutritional status, inflammation, and protein losses associated with dialysis

therapy.(10) Chronic inflammation may contribute to reduced albumin synthesis through inflammatory pathways, including cytokine-mediated regulation. (25, 26) In parallel, ongoing peritoneal protein losses may impose an additional catabolic burden that requires adequate nutritional compensation.(27) These processes are closely interrelated, as malnutrition and inflammation may reinforce each other and contribute to progressive loss of physiological reserve.(28)

Diabetes mellitus was independently associated with higher mortality in our time-dependent model (HR = 1.777; 95% CI, 1.395–2.262), consistent with previous time-dependent analyses in PD populations. (29, 30) This association likely reflects the complex metabolic, inflammatory, and vascular consequences of diabetes in patients with kidney failure. The monotonic dose–response relationship observed in spline analysis further supports the interpretation of serum albumin as a composite marker of overall biological vulnerability rather than solely a measure of nutritional status. (10, 28)

Time-dependent Cox modelling provides a methodological framework that addresses an important limitation of conventional baseline analyses by treating serum albumin as a dynamic exposure rather than a fixed baseline characteristic. A single albumin measurement at study entry represents only one point in the longitudinal trajectory of nutritional and inflammatory status, which may fluctuate in response to infection, hospitalization, dietary changes, and alterations in peritoneal transport characteristics. (14, 18)

By incorporating repeated albumin measurements from 1,680 patients, the time-dependent approach accounts for within-patient changes in serum albumin during follow-up. The model demonstrated good discrimination (C-index = 0.8176) and an AIC of 3487.22. A conventional baseline analysis was also performed in a smaller complete-case cohort of 1,094 patients, among whom 159 deaths occurred. Although the present study did not directly establish the incremental predictive value of time-varying albumin over baseline albumin, longitudinal assessment may reduce exposure misclassification associated with relying on a single baseline measurement. (14, 31)

Previous studies in dialysis populations have consistently demonstrated an association between lower serum albumin and adverse outcomes; however, most investigations have relied on baseline or cross-sectional measurements. Studies in haemodialysis populations have suggested that time-varying albumin assessment may better capture longitudinal mortality risk than single measurements, with attenuation of hazard estimates after accounting for temporal changes in albumin levels. (14, 31)

Comparable evidence in PD populations remains limited despite the substantial haemodialysis literature. (15, 17) In our cohort, the association between time-varying serum albumin and mortality was consistent with previous findings, although differences in effect estimates may reflect differences in dialysis modality, patient characteristics, and underlying nutritional–inflammatory states. Unlike some haemodialysis studies reporting J-shaped associations,(15) our spline analysis demonstrated a monotonic inverse association without evidence of statistical nonlinearity or a U-shaped pattern. These findings may reflect differences in nutritional management, dietary patterns, inflammatory profiles, and modality-specific pathophysiology.(5, 32, 33)

Serial monitoring of serum albumin may provide clinically relevant information that cannot be fully captured by a single baseline measurement. Identification of patients with low or declining albumin levels may prompt comprehensive assessment of nutritional status, inflammatory conditions, dietary intake, and potential peritoneal protein losses. The absence of evidence for statistical nonlinearity suggests that the association between albumin and mortality was not restricted to a particular nonlinear pattern within the observed range. The time-dependent modelling framework applied in this study may also be extended to other longitudinally changing biomarkers in PD populations, including dialysis adequacy parameters, residual kidney function, and inflammatory markers.

This study has several strengths. The longitudinal design with repeated measurements captures temporal variation in serum albumin more comprehensively than an analysis based solely on a single baseline measurement. The time-dependent Cox modelling approach allows changes in albumin during follow-up to be incorporated into the exposure definition and may reduce exposure misclassification inherent in baseline exposure assessment. The use of clustered robust standard errors accounts for the correlation arising from multiple observations per patient.(34) The restricted cubic spline analysis further characterized the shape of the association and demonstrated a predominantly monotonic inverse pattern across the observed albumin range.

Several limitations should be acknowledged. First, this was a single-centre retrospective study, which may limit generalizability to other PD populations. Second, residual confounding from unmeasured factors, including changes in dialysis prescription, medication use, and acute intercurrent illnesses, cannot be excluded. Although the time-dependent approach addresses limitations associated with fixed baseline exposure assessment, it does not eliminate potential bias from unmeasured time-varying confounders.

A proportion of patients were excluded during construction of the Andersen–Gill counting-process dataset because they could not contribute a valid risk interval. Specifically, 39 patients were excluded at this stage, including 9 patients whose death events could not be assigned to valid observation intervals and 30 patients with non-constructable or otherwise invalid longitudinal observation intervals. These exclusions represented approximately 2.3% of the 1,719 patients remaining after the preceding follow-up validation step. Although the proportion was relatively small, selection bias cannot be completely excluded.

Third, external validation of the model was not performed, and confirmation in independent multicentre cohorts is required. Finally, although the proportional hazards assumption was evaluated using Schoenfeld residuals, potential model misspecification and unmeasured time-varying confounding cannot be completely excluded. The findings should therefore be interpreted as an observational association rather than evidence of a causal effect of serum albumin on mortality.

Conclusion

In conclusion, time-varying serum albumin was independently associated with all-cause mortality among patients undergoing peritoneal dialysis. Incorporating serial albumin measurements into a time-dependent Cox proportional hazards model allowed longitudinal variation in serum albumin to be considered in the assessment of mortality risk. The observed monotonic inverse association between serum albumin and mortality, without evidence of statistical nonlinearity, supports serum albumin as an integrated marker reflecting nutritional and inflammatory status in patients receiving peritoneal dialysis. These findings highlight the potential value of serial serum albumin assessment as a component of longitudinal risk stratification in PD care.

Declarations

Ethical considerations

This study was approved by the Ethics Committee of Gaozhou People's Hospital (approval number: GYLLPJ-2025115). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate

The requirement for informed consent to participate was waived by the Ethics Committee of Gaozhou People's Hospital because of the retrospective nature of the study and the use of anonymised clinical data.

Consent for publication

Not applicable. This study used anonymised clinical data and did not contain identifiable individual information.

Conflicts of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Author Contribution

Yuping Sun and Liling Chen conceived and designed the study. Yuping Sun was responsible for data curation, statistical analysis, data analysis, interpretation of the results, and drafting the manuscript. Liling Chen contributed to study design, data analysis, interpretation of the findings, and critical revision

of the manuscript. Chuchu Chen and Miaotong Huang contributed to data collection, data curation, and manuscript revision. Jiayi Chen and Danni Liu contributed to data collection, statistical analysis, and interpretation of the results. Qiqi Huang contributed to data collection, data curation, and manuscript revision. Shanshan Deng contributed to interpretation of the results, scientific guidance, and critical revision of the manuscript. Wenxue Hu supervised the study, provided scientific guidance, and critically revised the manuscript. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Data Availability

The data that support the findings of this study are available from Gaozhou People's Hospital, but restrictions apply to the availability of these data, which were used under licence for the current study and are therefore not publicly available. The data are available from the corresponding author upon reasonable request and with permission of Gaozhou People's Hospital.

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Figures

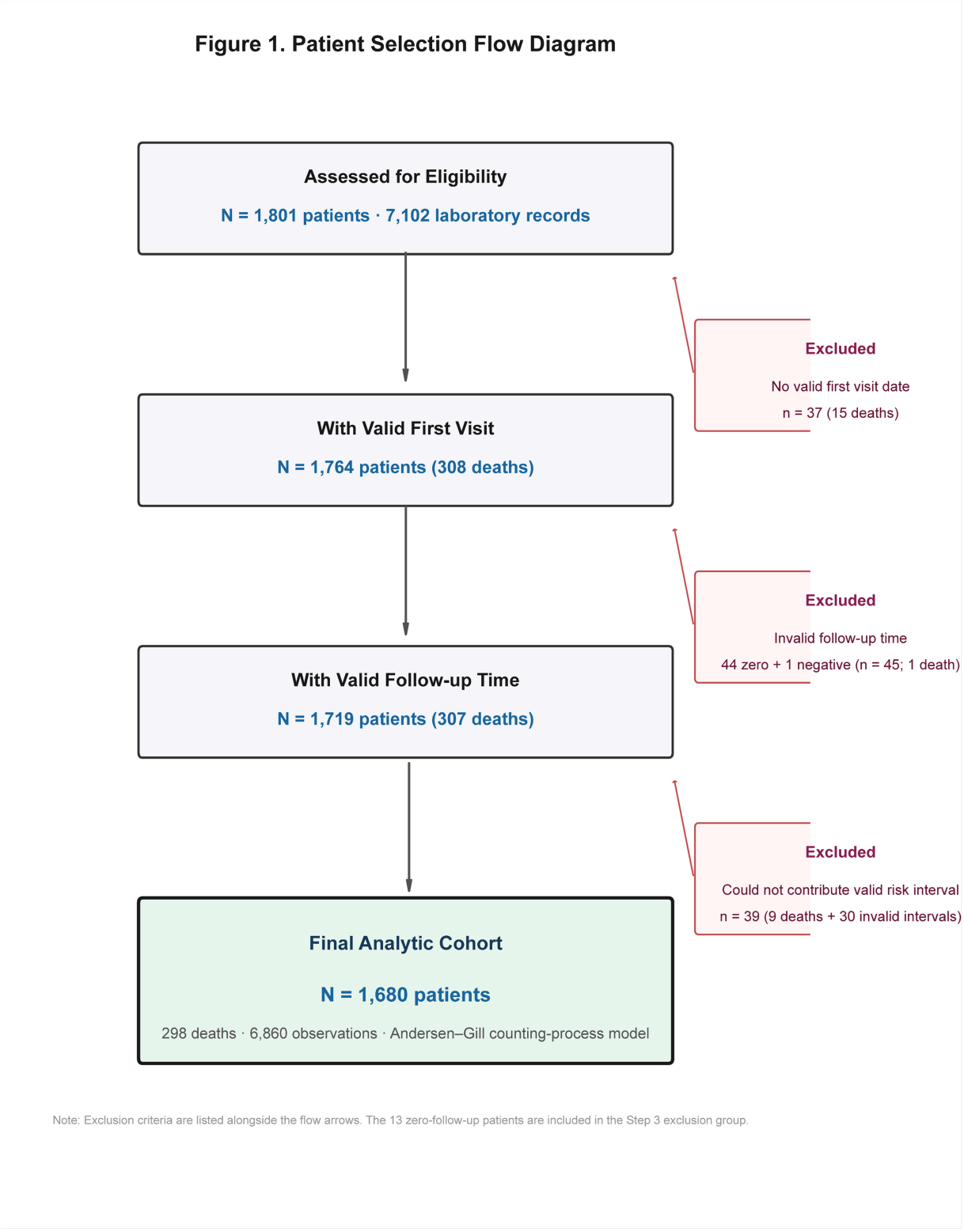


Figure 1

Patient selection flow diagram. Flow diagram illustrating the derivation of the final time-dependent Cox proportional hazards analysis cohort from the initial peritoneal dialysis database. Of 7,102 laboratory records from 1,801 unique patients, 37 patients without a valid first laboratory or visit date were excluded, leaving 1,764 patients. A further 45 patients were excluded because of invalid follow-up time, including zero or negative follow-up and one patient whose recorded detection date occurred after the

date of death, leaving 1,719 patients with valid follow-up. An additional 39 patients were excluded because they could not contribute a valid risk interval required for the Andersen–Gill counting-process analysis, including 9 patients whose death events could not be assigned to valid observation intervals and 30 patients with non-constructable or otherwise invalid longitudinal observation intervals. The final analytic cohort comprised 1,680 patients, contributing 6,860 observations to the fitted time-dependent Cox model and experiencing 298 all-cause death events.

Figure 2 Baseline characteristics of the study population according to survival status

Continuous variables presented as median (interquartile range) or mean ± standard deviation; categorical variables as n (%)

Variable	Alive (N = 1,478)	Deceased (N = 323)	Overall (N = 1,801)	P value*
Age, years	56.0 (44.0-62.0)	63.0 (57.0-71.0)	57.0 (46.0-64.0)	<0.001
PD vintage, months	15.5 (5.0-28.0)	13.2 (6.0-24.0)	15.0 (5.5-27.0)	0.241
Serum albumin, g/L	34.4 (30.5-38.0)	31.7 (28.1-35.3)	33.8 (30.0-37.6)	<0.001
C-reactive protein, mg/L	4.8 (1.3-15.5)	7.0 (1.9-19.3)	5.0 (1.5-16.5)	0.011
Hemoglobin, g/L	80.0 (69.0-93.0)	83.5 (71.0-95.0)	80.0 (69.0-93.0)	0.019
Blood urea nitrogen, mmol/L	23.4 (15.6-32.8)	19.2 (12.5-27.6)	22.8 (14.9-32.2)	<0.001
Serum creatinine, umol/L	779.0 (618.5-978.0)	677.0 (524.2-864.8)	762.8 (602.0-961.5)	<0.001
Calcium, mmol/L	2.0 (1.8-2.1)	2.0 (1.8-2.1)	2.0 (1.8-2.1)	0.750
Phosphorus, mmol/L	1.7 (1.3-2.2)	1.5 (1.1-1.9)	1.7 (1.3-2.2)	<0.001
Intact parathyroid hormone, pg/mL	344.0 (231.9-500.1)	243.9 (156.2-394.6)	330.8 (216.9-487.8)	<0.001
White blood cell count, x10^9/L	6.7 (5.4-8.8)	6.9 (5.4-8.6)	6.8 (5.4-8.7)	0.539
Neutrophil count, x10^9/L	4.8 (3.6-6.5)	4.8 (3.6-6.4)	4.8 (3.6-6.4)	0.857
Lymphocyte count, x10^9/L	1.1 (0.8-1.5)	1.1 (0.8-1.5)	1.1 (0.8-1.5)	0.507
Platelet count, x10^9/L	205.0 (157.0-255.0)	204.5 (160.2-257.0)	205.0 (157.0-255.2)	0.852
Neutrophil-to-lymphocyte ratio	4.2 (3.1-6.2)	4.3 (3.1-6.1)	4.2 (3.1-6.2)	0.772
Prognostic nutritional index	40.1 +/- 6.0	37.7 +/- 5.7	39.7 +/- 6.0	<0.001
Male, n (%)	842 (57.0%)	185 (57.3%)	1,027 (57.0%)	0.969
Diabetes, n (%)	347 (23.5%)	136 (42.1%)	483 (26.8%)	<0.001

**P values calculated using Wilcoxon rank-sum test for continuous variables, chi-square test for categorical variables.*

PD = peritoneal dialysis; IQR = interquartile range; SD = standard deviation.

Figure 2

Comparison of baseline characteristics between survivors and deceased patients in the full study cohort. Baseline characteristics were compared between survivors (N=1,478) and deceased patients (N=323) from the full cohort (N=1,801). Continuous variables are presented as median (interquartile range) or mean (standard deviation), according to the results of the Shapiro–Wilk test for normality. Categorical variables are presented as number (percentage). *P*-values were calculated using the Wilcoxon rank-sum test or Student's *t*-test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate. Abbreviations: ALB, albumin; BUN, blood urea nitrogen; CRP, C-

reactive protein; DM, diabetes mellitus; iPTH, intact parathyroid hormone; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; PD, peritoneal dialysis.

Figure 3. Forest plot of the time-dependent Cox proportional hazards model

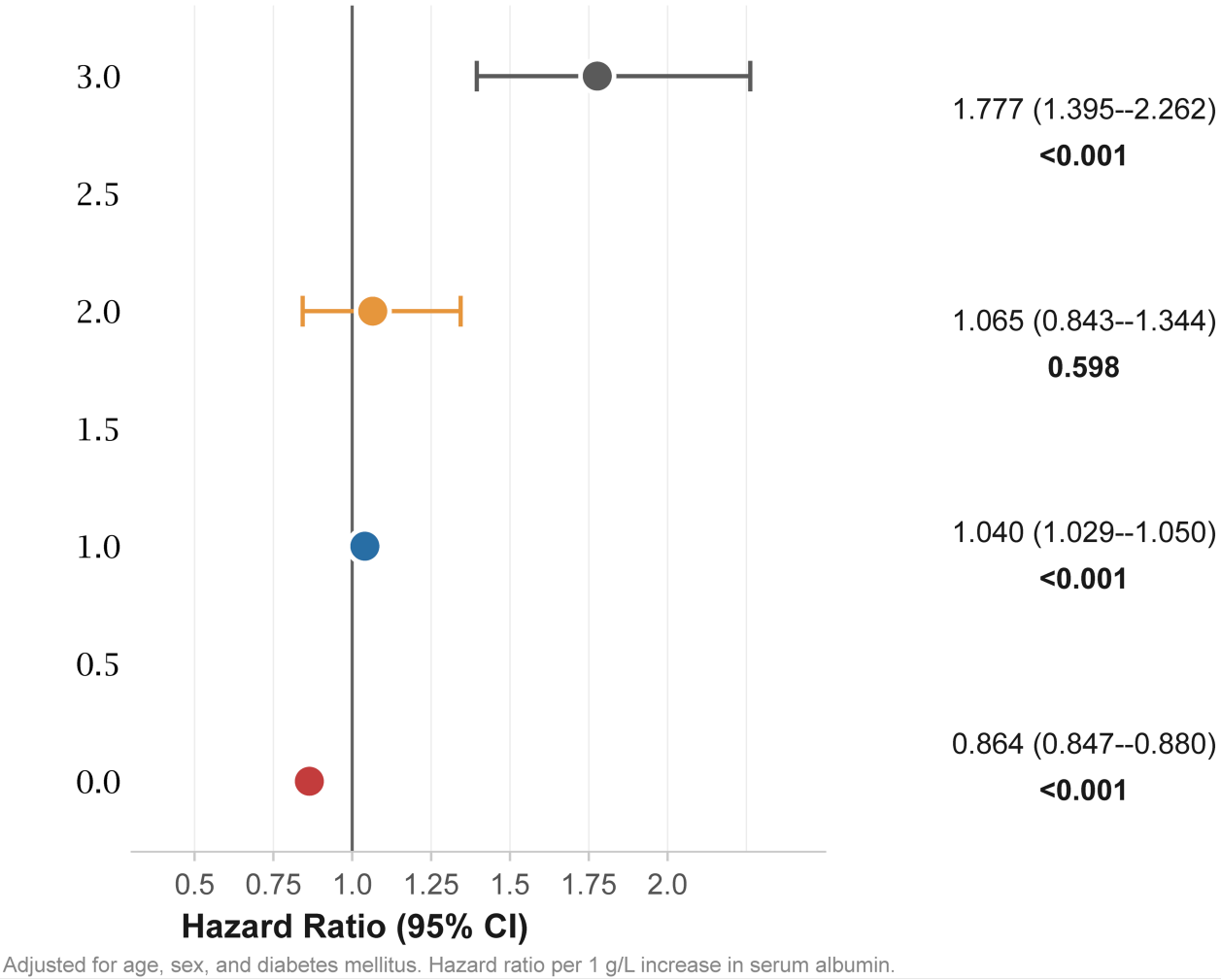


Figure 3

Forest plot of the time-dependent Cox proportional hazards model. Hazard ratios (HRs) and 95% confidence intervals (CIs) for serum albumin, age, sex, and diabetes mellitus from the time-dependent Cox model are shown. Each square represents the point estimate, and the horizontal line represents the corresponding 95% CI. The vertical dashed line denotes the null value (HR=1.0). HRs are presented per 1 g/L increase in serum albumin, per 1-year increase in age, for male versus female sex, and for diabetes mellitus versus no diabetes mellitus. The model was adjusted for age, sex, and diabetes mellitus. Abbreviations: CI, confidence interval; HR, hazard ratio.

Figure 4. Restricted cubic spline analysis of the dose--response relationship between serum albumin and all-cause mortality

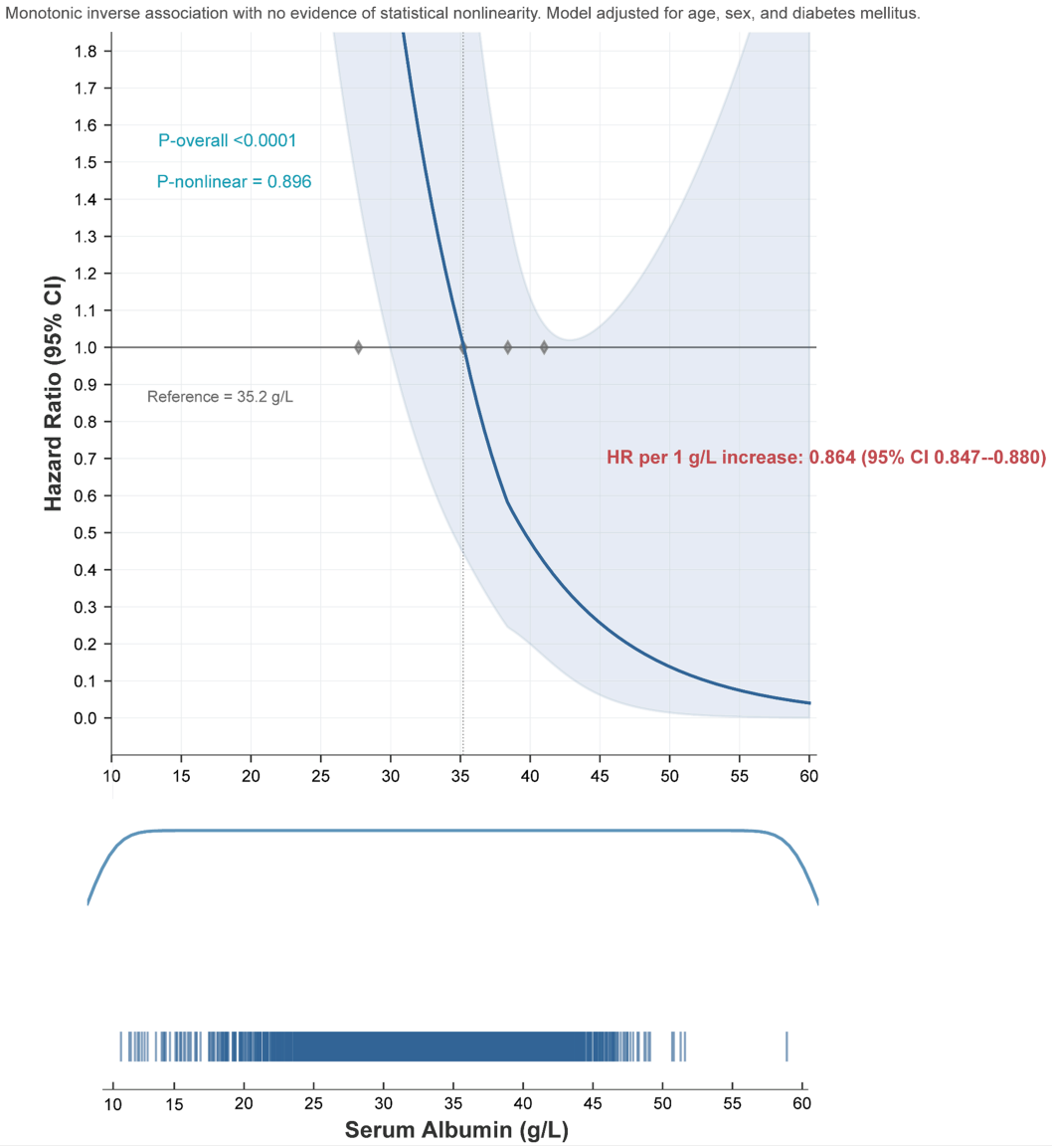
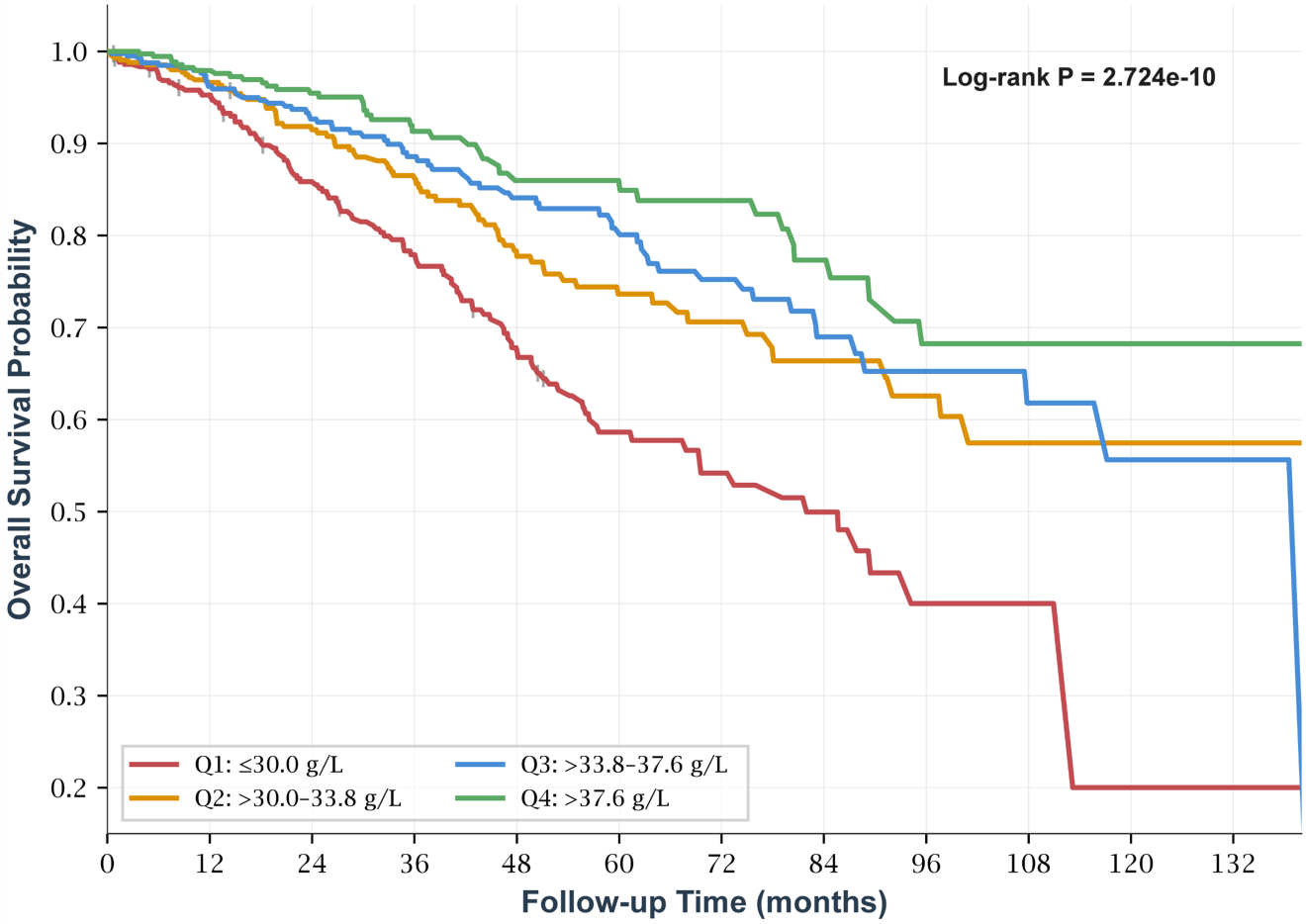


Figure 4

Restricted cubic spline analysis of the association between serum albumin and all-cause mortality. The solid line represents the adjusted hazard ratio, and the shaded area represents the 95% confidence interval across the observed serum albumin range (11.4–59.4 g/L). The vertical dotted line denotes the reference serum albumin level of 35.2 g/L (HR=1.0). Restricted cubic spline knots were placed at the 10th, 50th, 75th, and 90th percentiles (27.7, 35.2, 38.4, and 41.0 g/L, respectively). The overall association was statistically significant (*P*-overall<0.0001), whereas the test for nonlinearity was not significant (*P*-nonlinear=0.8962), indicating no statistical evidence of a nonlinear association. The model was adjusted for age, sex, and diabetes mellitus. Abbreviations: HR, hazard ratio.

Figure 5. Kaplan--Meier survival curves stratified by serum albumin quartiles



Q1	Q2	Time (months)	Q3	Q4
429	424	0	419	408
344	336	12	333	304
245	263	24	265	236
188	198	36	194	143
127	131	48	154	106
75	94	60	112	82
43	60	72	77	61
10	30	96	29	28
1	8	120	7	4

Figure 5

Kaplan–Meier survival curves stratified by baseline serum albumin quartiles. Patients were categorized according to the baseline serum albumin distribution into four groups: Q1 (≤30.0 g/L), Q2 (>30.0–33.8 g/L), Q3 (>33.8–37.6 g/L), and Q4 (>37.6 g/L). The shaded areas represent 95% confidence intervals. The log-rank test demonstrated a statistically significant difference in survival among the four groups

(P<0.001). The number of patients at risk at each time point is shown below the x-axis. Abbreviation: ALB, albumin.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterials.xlsx