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# Pretransplant C-reactive protein-to-albumin ratio predicts mortality in kidney transplant recipients: a retrospective cohort study

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**Background:** The C-reactive protein (CRP)-to-albumin ratio (CAR) is a more effective prognostic indicator than CRP or albumin alone in various diseases. This study aimed to evaluate the predictive value of the CAR for mortality in kidney transplant recipients (KTRs).
**Methods:** A total of 924 patients who underwent their first kidney transplantation at Kyungpook National University Hospital during 2006–2020 were enrolled and classified into quartile (Q) groups according to their pretransplant CAR values. A Cox regression analysis was conducted to analyze the hazard ratios (HRs) of mortality.
**Results:** Fifty-nine patients died during the posttransplant period (mean, 85.2±44.2 months). All-cause mortality (Q1, 3.0%; Q2, 4.8%; Q3, 7.8%; Q4, 10.0%; P for trend <0.001) and infection-related mortality increased linearly with an increase in CAR (P for trend=0.004). The Q3 and Q4 had higher risks of all-cause mortality than Q1 after adjusting for confounding factors (Q3: adjusted HR [aHR] 2.49, 95% confidence interval [CI] 1.04–5.99, P=0.041; Q4: aHR 3.09, 95% CI 1.31–7.27, P=0.010). Q4 was also independently associated with infection-related mortality (aHR 5.83, 95% CI 1.27–26.8, P=0.023). The area under the curve of the CAR for all-cause and infection-related mortality was higher than that of CRP or albumin alone. There was no association between CAR and death-censored graft failure or acute rejection.
**Conclusions:** A higher pretransplant CAR increases the risk of posttransplant mortality, particularly infection-related, in KTRs. Pretransplant CAR can be an effective and easily accessible predictor of posttransplant mortality.

**Keywords:** Albumin; C-reactive protein; C-reactive protein-to-albumin ratio; Kidney transplantation; Mortality

## HIGHLIGHTS

- The C-reactive protein-to-albumin ratio (CAR) has been identified as a useful prognostic marker in various fields, but no study has evaluated its role in kidney transplant recipients.
- This single-center, retrospective cohort study confirmed a significant association between pretransplant CAR and the risk of mortality in kidney transplant recipients.
- In particular, high pretransplant CAR was associated with an increased risk of infection-related death.
- No association was found between CAR and death-censored graft failure or the occurrence of acute rejection.

## INTRODUCTION

Kidney transplantation (KT) is the most preferred treatment for patients with end-stage kidney disease (ESKD), and it contributes greatly to improving their quality of life and survival [1,2]. Although kidney transplant recipients (KTRs) have better survival than dialysis patients, they have higher mortality rates than the general population [3,4]. This is because KTRs have various comorbidities, such as diabetes and cardiovascular disease, and they need to take immunosuppressive agents, which increase the risk of infections and malignancies [5,6].

Several studies have identified parameters to predict the prognosis of KTRs [7-9]. However, these prognostic indicators have limitations, such as inconsistent results, high costs, and low predictive power [10]. Many researchers have recently been interested in easily accessible prognostic indicators and have investigated the roles of biological markers such as C-reactive protein (CRP) and albumin in predicting short- and long-term prognoses in various diseases [11,12].

CRP is a sensitive parameter that is elevated in various diseases such as infections, tumors, and autoimmune diseases [13]. Albumin is a useful marker of nutritional status, which sensitively decreases not only in catabolic statuses such as acute infection, liver cirrhosis, and malignant disease but also in various kidney diseases with proteinuria [14,15]. CRP and albumin are both well-known as reliable prognostic indicators that predict morbidity and mortality in patients on dialysis [16,17]. Furthermore, many studies have evaluated the association between the CRP-to-albumin ratio (CAR) and prognosis because CRP or albumin levels alone can be relatively non-specific [18]. The CAR was identified as an independent predictor of all-cause mortality in ESKD patients on peritoneal dialysis [19].

Many patients with chronic kidney disease (CKD) experience chronic inflammation and poor nutritional status. In addition, KTRs have an increased risk of infection because of their immunosuppressive state. Therefore, this study aimed to evaluate the predictive role of the pretransplant CAR for the prognosis after KT in patients with ESKD.

## METHODS

This study was approved by the Institutional Review Board of Kyungpook National University Hospital (IRB No. 2022-10-018). The requirement for informed consent was waived because this study was conducted through a retrospective review of medical records. All patient information was anonymized, and the patients were de-identified before analyses. This study was conducted in accordance with the 2013 Declaration of Helsinki and the Declaration of Istanbul 2008.

### Study Population

Patients who underwent KT for the first time at Kyungpook National University Hospital between January 2006 and August 2020 were retrospectively analyzed. Patients who had signs of infection or a history of albumin infusion within 2 weeks prior to KT were excluded. We divided the enrolled patients into quartile (Q) groups according to the pretransplant CAR values. During hospitalization for KT, all patients were managed according to the institution's perioperative protocols [20]. This included routine laboratory and radiologic examinations, immunological management, desensitization treatment if needed, and proper surgical procedures.

### Data Collection

The baseline demographic data included information on both the recipient and the donor. The recipient characteristics included age, sex, body mass index (BMI), follow-up duration after KT, dialysis vintage before KT, primary causes of renal disease, comorbid conditions, number of human leukocyte antigen (HLA) mismatches,



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and induction immunosuppressive agents, while the donor characteristics included age, sex, and BMI. This data was collected by reviewing electronic medical records. In all KTRs, blood samples were collected 24 hours before KT, and this study analyzed the samples collected at the nearest time point before the KT. The serum laboratory parameters included white blood cell (WBC) count, neutrophil count, lymphocyte count, hemoglobin, platelet count, sodium, potassium, calcium, phosphate, uric acid, total/low-density lipoprotein (LDL) cholesterol, CRP, and albumin. The CAR was calculated as a percentage (CRP/albumin ×100).

**Outcomes**

The primary outcome was mortality according to the CAR. Patient deaths were categorized into infection, cardiovascular, and cancer-related deaths. The secondary outcomes were the occurrence of death-censored graft failure and biopsy-proven acute rejection (BPAR) during the observation period. The predictive role of CRP or albumin alone for mortality was assessed and compared to that of the CAR. Patient survival was defined as the time from transplantation to death due to any cause. Death-censored graft failure was defined as an event in which graft function was aggravated, leading to the re-initiation of renal replacement therapy [20]. In the case of patients who died with a functioning graft, the patient's graft survival was censored at the time of death. BPAR was diagnosed according to the Banff 2007 classification [21]. When the Banff classification was updated later, BPAR was diagnosed accordingly. Graft biopsy was performed considering the clinical findings such as a decline of graft function or suspicion of BK virus nephropathy.

**Statistical Analysis**

The results of normally distributed continuous variables are expressed as means and standard deviations. The results of those non-normally distributed continuous variables are expressed as medians and interquartile ranges (IQRs), and the results of categorical variables are expressed as numbers (percentages). One-way analysis of variance or the Kruskal-Wallis test for continuous variables and the chi-square test for categorical variables were used to compare differences among quartiles. The Cochrane-Armitage trend test was performed to analyze the trend in the percentage of patients who experienced clinical outcome events, such as death, death-censored graft failure, and BPAR. Patient survival, graft survival, and BPAR-free survival were analyzed using Kaplan-Meier curves, and the log-rank test was used to confirm differences between groups. Univariate and multivariate Cox proportional hazard regression models were used to calculate the hazard ratio (HR) and 95% confidence interval (CI) for patient death, death-censored graft failure, and BPAR. Several variables in the baseline characteristics were adjusted in the multivariate Cox regression analysis: model 2 adjusted for age, sex, and BMI; model 3 adjusted for the model 2 variables, dialysis vintage, comorbid diabetes, and donor type; and model 4 adjusted for the model 3 variables, neutrophil count, hemoglobin, and platelet count. Receiver operating characteristic (ROC) curve and area under the curve (AUC) analyses were performed to determine the predictive performance of the parameters for patient death. All statistical analyses were conducted using IBM SPSS ver. 22 (IBM Corp.) and R (ver. 3.6.2; The R Foundation for Statistical Computing). The statistical significance threshold was set at $P<0.05$.

## RESULTS

**Baseline Characteristics**

In total, 924 KTRs were included in this study. The mean age of patients was 46.8±12.4 years, and 61.7% of them were male. The mean follow-up duration after KT was 85.2±44.2 months. The median CAR value was 2.50% (IQR, 1.11%–7.23%), and the ranges in the Qs were as follows: Q1, CAR <1.12%; Q2, CAR ≥1.12 and <2.52%; Q3, CAR ≥2.52% and <7.25%; Q4, CAR ≥7.25%. The baseline characteristics according to CAR Qs are shown in Table 1. The proportion of male patients was higher in the higher Qs (Q3 and Q4) than in the lower Qs (Q1 and Q2; $P<0.001$); a similar trend was noted for baseline BMI ($P<0.001$). There were no significant differences in age distribution, follow-up duration, pretransplant dialysis vintage, primary renal disease, comorbid hypertension, and diabetes. The immunologic characteristics, such as the number of HLA mismatches, desensitization, and type of induction immunosuppressive agent, were also not significantly different. The proportion of living donor KT was higher in the lower quartiles than in the higher quartiles ($P<0.001$). Among the laboratory findings, the WBC count, neutrophil count, and CRP level were the highest in Q4 and the lowest in Q1 ($P<0.001$); the LDL cholesterol level was the highest in Q1 and the lowest in Q4 ($P=0.027$).

**Table 1.** Baseline characteristics

| Characteristic | Quartile | | | | P-value |
|---|---|---|---|---|---|
| | 1 (n=232) | 2 (n=231) | 3 (n=231) | 4 (n=230) | |
| Age (yr) | 46.3±12.2 | 46.4±12.1 | 47.3±12.3 | 47.4±12.8 | 0.658 |
| Male sex | 126 (54.3) | 128 (55.4) | 152 (65.8) | 164 (71.3) | <0.001 |
| Body mass index (kg/m$^2$) | 21.5±3.0 | 22.3±3.2 | 22.7±3.5 | 22.8±13.3 | <0.001 |
| Follow-up duration after KT (mo) | 89.4±40.9 | 81.9±50.0 | 84.5±44.5 | 84.9±40.6 | 0.339 |
| Dialysis vintage before KT (mo) | 12.0 (0.0–62.8) | 13.0 (0.0–72.1) | 24.5 (1.3–90.0) | 17.4 (0.0–87.2) | 0.051 |
| Primary renal disease | | | | | 0.261 |
| Glomerulonephritis | 143 (61.6) | 132 (57.1) | 125 (54.1) | 119 (51.7) | |
| Diabetes | 51 (22.0) | 71 (30.7) | 74 (32.0) | 73 (31.7) | |
| Hypertension | 17 (7.3) | 12 (5.2) | 18 (7.8) | 17 (7.4) | |
| Other | 21 (9.1) | 16 (6.9) | 14 (6.1) | 21 (9.1) | |
| Comorbid conditions | | | | | |
| Hypertension | 194 (83.6) | 193 (83.5) | 192 (83.1) | 176 (76.5) | 0.136 |
| Diabetes | 59 (25.4) | 81 (35.1) | 82 (35.5) | 79 (34.3) | 0.064 |
| Number of HLA mismatches | 3.2±1.6 | 3.2±1.6 | 3.1±1.7 | 3.0±1.8 | 0.402 |
| Number of HLA-DR mismatches | 1.1±0.7 | 1.0±0.7 | 1.1±0.7 | 1.0±0.7 | 0.675 |
| Desensitization | 37 (15.9) | 39 (16.9) | 34 (14.7) | 30 (13.0) | 0.686 |
| Induction immunosuppressant | | | | | 0.511 |
| Anti-thymocyte globulin | 13 (5.6) | 17 (7.4) | 10 (4.3) | 16 (7.0) | |
| Basiliximab | 219 (94.4) | 214 (92.6) | 221 (95.7) | 214 (93.0) | |
| Donor age (yr) | 46.4±13.7 | 46.8±13.3 | 47.3±14.6 | 45.9±13.0 | 0.748 |
| Donor sex (male) | 121 (52.6) | 116 (50.2) | 126 (55.5) | 125 (54.6) | 0.678 |
| Donor body mass index (kg/m$^2$) | 23.1±3.3 | 23.6±3.4 | 23.7±3.2 | 23.8±3.4 | 0.158 |
| Donor type | | | | | 0.001 |
| Living | 150 (64.7) | 166 (71.9) | 132 (57.1) | 129 (56.1) | |
| Deceased | 82 (35.3) | 65 (28.1) | 99 (42.9) | 101 (43.9) | |
| Laboratory finding | | | | | |
| WBC count (×10$^9$/L) | 5.56 (4.50–7.28) | 6.07 (4.93–7.79) | 6.18 (4.67–7.39) | 6.43 (5.06–8.09) | <0.001 |
| Neutrophil count (×10$^9$/L) | 3.53 (2.63–4.93) | 3.88 (3.05–5.42) | 3.75 (2.78–5.18) | 4.19 (3.22–5.56) | 0.002 |
| Lymphocyte count (×10$^9$/L) | 1.18 (0.86–1.53) | 1.17 (0.91–1.62) | 1.25 (0.93–1.59) | 1.27 (0.95–1.68) | 0.201 |
| Hemoglobin (g/dL) | 10.4 (9.3–11.4) | 10.9 (9.5–11.9) | 10.7 (9.5–11.9) | 10.4 (9.2–11.6) | 0.015 |
| Platelet count (×10$^9$/L) | 173.0 (134.5–212.5) | 182.0 (147.0–228.0) | 189.0 (147.0–236.0) | 198.0 (157.0–250.3) | <0.001 |
| Sodium (mEq/L) | 138.0 (136.0–141.0) | 138.0 (136.0–140.0) | 138.0 (135.0–140.0) | 137.0 (135.0–139.0) | 0.058 |
| Potassium (mEq/L) | 4.6±0.8 | 4.5±0.8 | 4.6±0.8 | 4.5±0.9 | 0.101 |
| Calcium (mg/dL) | 8.7 (8.1–9.4) | 8.9 (8.1–9.4) | 8.8 (8.2–9.5) | 8.8 (8.1–9.4) | 0.679 |
| Phosphate (mg/dL) | 4.7 (3.9–5.7) | 4.8 (3.9–5.9) | 4.9 (3.9–6.0) | 5.1 (3.9–6.1) | 0.618 |
| Uric acid (mg/dL) | 5.0 (4.0–7.2) | 4.6 (3.5–6.4) | 5.3 (4.0–6.7) | 5.4 (4.0–6.6) | 0.010 |
| Total cholesterol (mg/dL) | 155.7±39.5 | 157.9±42.6 | 152.4±44.1 | 154.0±44.9 | 0.905 |
| LDL cholesterol (mg/dL) | 96.5±33.4 | 93.9±32.1 | 91.9±36.7 | 82.9±25.7 | 0.027 |
| CRP (mg/dL) | 0.02 (0.01–0.04) | 0.08 (0.06–0.10) | 0.16 (0.12–0.22) | 0.53 (0.29–1.08) | <0.001 |
| Albumin (g/dL) | 4.1 (3.8–4.5) | 4.2 (3.7–4.5) | 4.0 (3.5–4.4) | 3.7 (3.3–4.2) | <0.001 |
| CAR | 0.60 (0.31–0.91) | 1.88 (1.49–2.27) | 4.19 (3.13–5.73) | 13.48 (8.53–30.26) | <0.001 |

Values are presented as mean±standard deviation, number (%), or median (interquartile range). Quartile groups were established by dividing patients based on pretransplant CAR values.

KT, kidney transplantation; HLA, human leukocyte antigen; WBC, white blood cells; LDL, low-density lipoprotein; CRP, C-reactive protein; CAR, C-reactive protein-to-albumin ratio.



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**Table 2.** The incidence of patient death, death-censored graft failure, and biopsy-proven acute

| Variable | Quartile | | | | P-value |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | |
| Patient death | 7 (3.0) | 11 (4.8) | 18 (7.8) | 23 (10.0) | 0.011 |
| Infection | 2 (0.9) | 4 (1.7) | 3 (1.3) | 12 (5.2) | 0.006 |
| Cardiovascular | 3 (1.3) | 4 (1.7) | 5 (2.2) | 3 (1.3) | 0.880 |
| Cancer | 1 (0.4) | 3 (1.3) | 6 (2.6) | 7 (3.0) | 0.112 |
| Other[a)] | 1 (0.4) | 0 | 4 (1.7) | 1 (0.4) | 0.141 |
| Hospitalization due to an infectious complication within 1 yr | 32 (13.8) | 28 (12.1) | 35 (15.2) | 49 (21.3) | 0.041 |
| Death-censored graft failure | 21 (9.1) | 17 (7.4) | 27 (11.7) | 24 (10.4) | 0.431 |
| BPAR | 23 (9.9) | 18 (7.8) | 24 (10.4) | 24 (10.4) | 0.743 |
| TCMR | 14 (6.0) | 11 (4.8) | 13 (5.6) | 17 (7.4) | 0.686 |
| ABMR | 10 (4.3) | 8 (3.5) | 12 (5.2) | 7 (3.0) | 0.651 |
| BPAR within 1 yr | 7 (3.0) | 5 (2.2) | 14 (6.1) | 7 (3.0) | 0.118 |

Values are presented as number (%). Quartile groups were established by dividing patients based on pretransplant C-reactive protein-to-albumin ratio values.

BPAR, biopsy-proven acute rejection; TCMR, T cell-mediated rejection; ABMR, antibody-mediated rejection.

[a)]The category of "other" indicates sudden cardiac arrest and trauma.

**Clinical Outcomes after Kidney Transplantation**

The incidence rates of patient death, death-censored graft failure, and BPAR are summarized in Table 2. There were 59 deaths during the follow-up period, and the mortality increased with increasing Q (Q1, 7 [3.0%]; Q2, 11 [4.8%]; Q3, 18 [7.8%]; Q4, 23 [10.0%]; P=0.011; P for trend <0.001). In the subgroup analysis, the incidence of infection-related death increased linearly according to an increase in the CAR (Q1, 2 [0.9%]; Q2, 4 [1.7%]; Q3, 4 [1.3%]; Q4, 12 [5.2%]; P=0.006; P for trend=0.004). Supplementary Table 1 shows the details of infection-related deaths; the incidence of pneumonia and bacterial infection was higher in Q4. In addition, the incidence of hospitalization due to infectious complications within the first year after KT was also higher in Q4 (Q1, 32 [13.8%]; Q2, 28 [12.1%]; Q3, 35 [15.2%]; Q4, 49 [21.3%]; P=0.041). However, cardiovascular death and cancer-related death did not differ significantly among the Q groups.

There were no significant differences in the incidence of death-censored graft failure or BPAR, including acute T cell-mediated rejection, active antibody-mediated rejection, and early BPAR, among the quartiles.

**Association between the CAR and Mortality and Graft Outcomes**

The Kaplan-Meier curves showed significant differences in the cumulative survival for all-cause and infection-related mortality according to CAR quartiles (log-rank P=0.011 and P=0.006, respectively) (Fig. 1A and B). However, the Kaplan-Meier curve for cardiovascular mortality did not differ significantly among the Q groups (log-rank P=0.816) (Fig. 1C).

Table 3 shows the results of the Cox proportional hazards regression analysis for all-cause mortality. Compared to Q1, the higher CAR groups, Q3 and Q4, had a consistently higher risk of all-cause death in all models (model 4; Q3: adjusted HR, 2.49; 95% CI, 1.04–5.99; P=0.041; Q4: adjusted HR, 3.09; 95% CI, 1.31–7.27; P=0.010). Table 4 shows the results of the Cox proportional hazard regression analysis for infection-related mortality. The Q4 had a consistently higher risk of infection-related death in all models compared to Q1 (model 4; Q4: adjusted HR, 5.83; 95% CI, 1.27–26.80; P=0.023).

The association between CAR groups and death-censored graft failure risk or BPAR risk was also analyzed. No significant relationships were found between the CAR Q and the risk of death-censored graft failure (Supplementary Table 2) or BPAR (Supplementary Table 3).

**Receiver Operating Characteristic Analysis for Mortality**

Fig. 2 shows a comparison of the ROC curves of the CAR, CRP, and albumin levels for mortality. For prediction of all-cause mortality, the CAR showed the highest AUC value (0.610; 95% CI, 0.578–0.642), followed by CRP (0.589; 95% CI, 0.556–0.621) and albumin (0.573; 95% CI, 0.541–0.605) (Fig. 2A). The cutoff value of the CAR for predicting

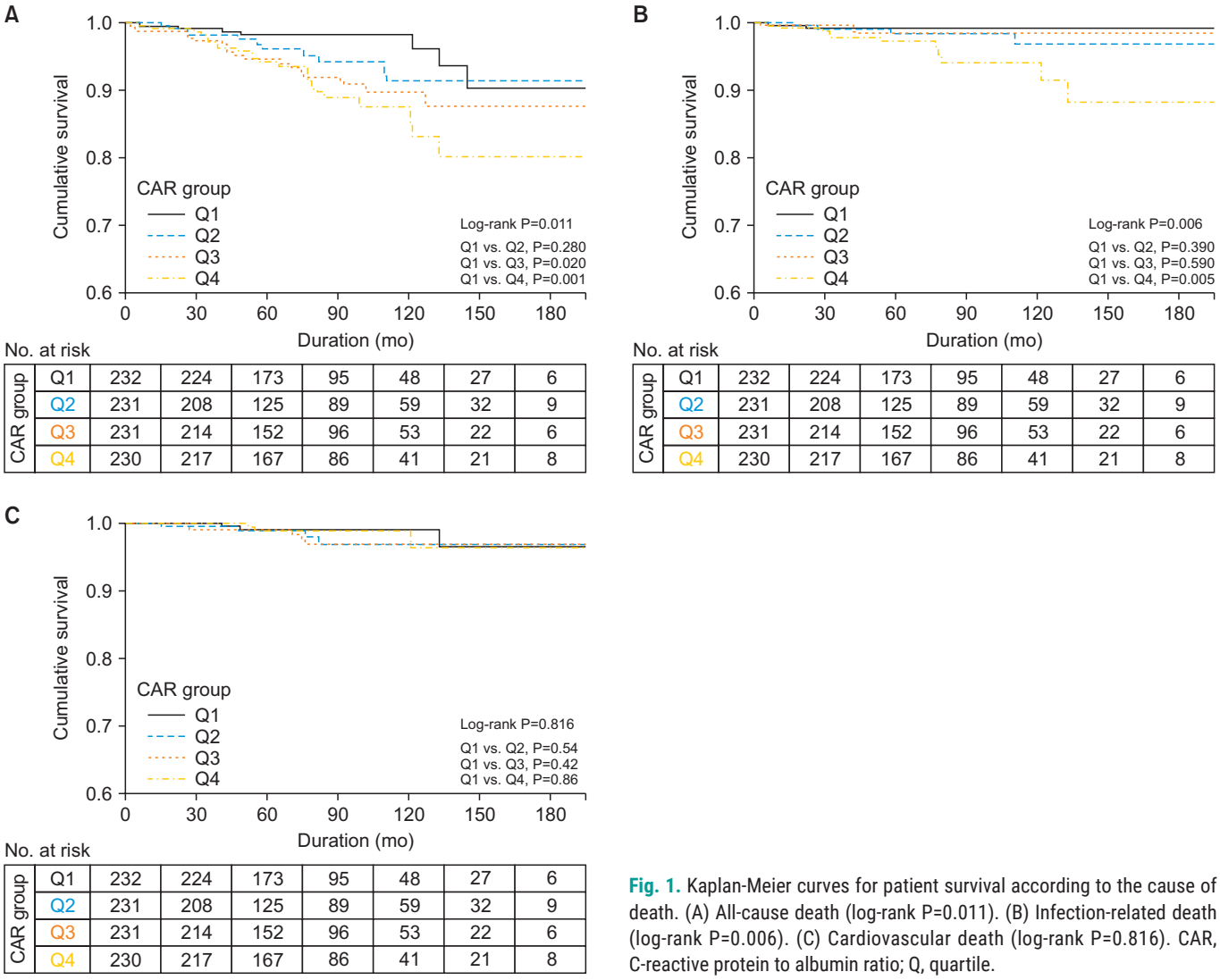


**Fig. 1.** Kaplan-Meier curves for patient survival according to the cause of death. (A) All-cause death (log-rank P=0.011). (B) Infection-related death (log-rank P=0.006). (C) Cardiovascular death (log-rank P=0.816). CAR, C-reactive protein to albumin ratio; Q, quartile.

all-cause mortality was >2.78%. To predict infection-related mortality, the CAR also showed the highest AUC value (0.678; 95% CI, 0.647–0.708), followed by albumin (0.675; 95% CI, 0.643–0.705) and CRP (0.636; 95% CI, 0.604–0.667) (Fig. 2B). The cutoff value of the CAR for predicting infection-related mortality was >7.40%.

## DISCUSSION

This study revealed a positive correlation between the pretransplant CAR and mortality after transplantation in KTRs. An elevated CAR was closely associated with an increased risk of infection-related death, whereas the CAR is not associated with cardiovascular death, death-censored graft failure, or BPAR. The CAR, which combines CRP and albumin, had better predictive power for mortality than CRP and albumin alone. To the best of our knowledge, this is the first study to show the predictive value of the CAR for mortality in KTRs.

Previous studies have reported the clinical usefulness of the CAR as a prognostic marker in patients with sepsis, critical illness, and ESKD [19,22]. These studies highlighted the link between inflammation and the CAR as the basis of the correlation. Chronic inflammatory conditions are highly prevalent in patients with advanced CKD, especially in those undergoing dialysis [23]. CRP is one of the most powerful markers of the innate immune system and is considered a clinically important acute-phase



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**Table 3.** The Cox proportional hazards regression model for all-cause mortality according to the C-reactive protein-to-albumin ratio quartile groups

| Quartile | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | P-value | aHR (95% CI) | P-value | aHR (95% CI) | P-value | aHR (95% CI) | P-value |
| 1 | Reference | - | Reference | - | Reference | - | Reference | - |
| 2 | 1.75 (0.68–4.51) | 0.250 | 1.87 (0.72–4.84) | 0.196 | 1.85 (0.71–4.78) | 0.207 | 1.85 (0.71–4.79) | 0.207 |
| 3 | 2.75 (1.15–6.58) | 0.023 | 2.56 (1.07–6.13) | 0.035 | 2.48 (1.03–5.95) | 0.042 | 2.49 (1.04–5.99) | 0.041 |
| 4 | 3.54 (1.52–8.25) | 0.003 | 3.16 (1.35–7.39) | 0.008 | 3.03 (1.29–7.09) | 0.011 | 3.09 (1.31–7.27) | 0.010 |

Model 1, unadjusted; Model 2, adjusted for age, sex, and body mass index; Model 3: adjusted for age, sex, body mass index, dialysis vintage, comorbid diabetes, and donor type; Model 4, adjusted for age, sex, body mass index, dialysis vintage, comorbid diabetes, donor type, neutrophil count, hemoglobin level, and platelet count.
HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio.

**Table 4.** The Cox proportional hazards regression model for infection-related mortality according to the C-reactive protein-to-albumin ratio quartile groups

| Quartile | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | P-value | aHR (95% CI) | P-value | aHR (95% CI) | P-value | aHR (95% CI) | P-value |
| 1 | Reference | - | Reference | - | Reference | - | Reference | - |
| 2 | 2.17 (0.40–11.89) | 0.370 | 2.27 (0.41–12.40) | 0.346 | 2.08 (0.38–11.47) | 0.400 | 2.12 (0.38–11.81) | 0.391 |
| 3 | 1.58 (0.26–9.47) | 0.615 | 1.50 (0.25–8.99) | 0.658 | 1.45 (0.24–8.74) | 0.682 | 1.48 (0.24–8.93) | 0.670 |
| 4 | 6.41 (1.44–28.66) | 0.015 | 5.98 (1.33–26.87) | 0.020 | 5.64 (1.25–25.43) | 0.024 | 5.83 (1.27–26.80) | 0.023 |

Model 1, unadjusted; Model 2, adjusted for age, sex, and body mass index; Model 3, adjusted for age, sex, body mass index, dialysis vintage, comorbid diabetes, and donor type; Model 4, adjusted for age, sex, body mass index, dialysis vintage, comorbid diabetes, donor type, neutrophil count, hemoglobin level, and platelet count.
HR, hazard ratio; CI, confidence intervals; aHR, adjusted hazard ratio.

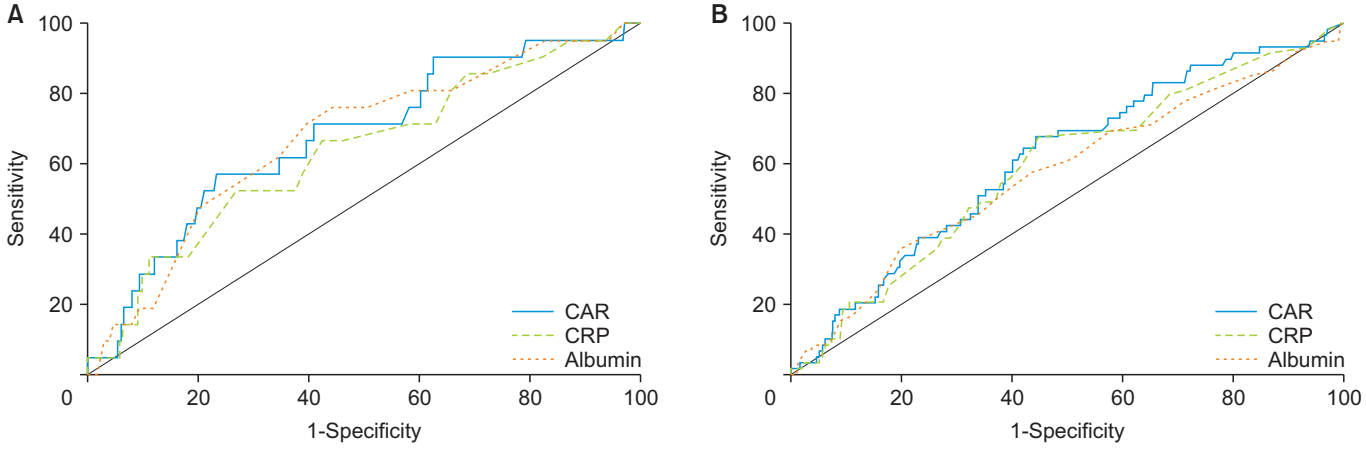


**Fig. 2.** Receiver operating characteristic curves of prognostic predictors for patient death. (A) All-cause mortality. The AUC values are as follows: CAR (0.610), CRP (0.589), albumin (0.573). The cutoff value of the CAR was over 2.78%. (B) Infection-related mortality. The AUC values are as follows: CAR (0.678), CRP (0.636), albumin (0.675). The cutoff value of the CAR was over 7.40%. CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; AUC, area under the curve.

marker of infection and inflammation [24]. In addition, a chronic inflammatory condition in patients with ESKD is closely correlated with the protein-energy wasting (PEW) syndrome [25]. PEW refers to the multiple nutritional and catabolic alterations in patients with CKD, and it has an impact on mortality and morbidity in CKD. Serum albumin level is the most representative indicator of PEW [26]. In this aspect, the CAR, which considers changes in CRP and

albumin levels together, can be a useful mortality indicator in KTRs.

Few studies have evaluated the predictive role of the CAR in the field of solid organ transplantation. Amygdalos et al. [18] reported the predictive performance of the CAR in liver transplant recipients (LTRs). The CAR is a reliable additional tool for predicting perioperative morbidity (which is measured by the Comprehensive Complication Index [27]) and mortality in deceased-donor LTRs. Another study from Korea also reported that overall mortality increased in the high-CAR group during the follow-up period in living-donor LTRs [28]. Our study showed similar results, supporting the CAR as a useful mortality-predictive marker for KTRs. In addition, no study has confirmed the predictive value of the CAR according to the cause of death in solid organ transplant recipients. For the first time, we identified that infection-related death, but not death from cardiovascular disease or other causes, was associated with the CAR.

Interestingly, both CRP and albumin are acute-phase proteins, but we confirmed that the CAR is associated with long-term mortality in KTRs. Since patients before KT did not have an acute illness, the absolute value of the CAR was generally much lower than that of patients with acute illness. CAR may be an index that reflects these stable patients' underlying characteristics, such as frailty and malnutrition, so it can predict long-term mortality.

The present study confirmed that the CAR is not associated with graft function in KTRs. Unlike KTRs, Park et al. [28] found that the CAR could predict early allograft dysfunction in living-donor LTRs. The predictive power of the CAR for allograft dysfunction was greater than that of other parameters, such as CRP or albumin alone, WBC count, and the neutrophil-to-lymphocyte ratio. This difference in predicting allograft function may be due to differences in immunosuppressant use, transplanted organs, and baseline patient characteristics between LTRs and KTRs. Altogether, the mortality and graft function results suggest that the risk of infection should be reduced in KTRs with a high CAR before transplantation by adjusting the dose of immunosuppressants after KT, and the development of infectious complications should be carefully monitored during follow-up.

Reliable tools for screening for vulnerability to infection and mortality before transplantation are scarce. Several inflammatory markers are upregulated in patients with CKD, including lymphocytes, tumor necrosis factor receptor 1, interleukin-1, and interleukin-6 [29]. The key features of a good prognostic marker are noninvasiveness, ease of measurement and interpretation, reproducibility, good prognostic performance, and cost-effectiveness [30]. The CAR, which comprises CRP and albumin, is an easily measurable, reproducible, and inexpensive parameter. Therefore, the CAR can be a good parameter for predicting the risk of death after KT, including infection-related death.

This study has several limitations. First, as this was an observational, retrospective, single-center study, selection bias may have been present and the related factors may not have been properly controlled. By using multivariate analysis, we tried to minimize the effect of confounding factors and correct statistical errors; however, we were not able to collect information on some unknown confounding factors. Second, since CRP and albumin are acute-phase proteins, it was difficult to clarify the causal relationship between pretransplant serum levels and events that occurred after a long period. Moreover, we used only CAR data before KT and did not consider serial changes in the CAR during the follow-up period. Third, this study focused on analyses of phenomena, such as the incidence of events, and the pathophysiological mechanisms underlying these events cannot be identified. Fourth, the CAR had a relatively low AUC, without statistically significant differences compared to the AUCs of CRP or albumin. Despite these limitations, this study is meaningful as it is the first to confirm the death-predictive performance of the CAR in KTRs. Based on the results of this study, prospective, multicenter, and large-scale follow-up studies are needed in the future.

In conclusion, KTRs with a high pretransplant CAR had an increased risk of all-cause mortality and infection-related mortality after KT. A high CAR was not associated with graft dysfunction or the occurrence of BPAR. The CAR can be a good predictor of mortality in KTRs, and precautions should be taken to reduce the risk of infectious complications in patients who had a high pretransplant CAR.

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**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.



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**Supplementary Materials**
Supplementary materials can be found via https://doi.org/10.4285/kjt.22.0047.

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