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Prognostic value of serum albumin in aortic
aneurysm patients undergoing graft
replacement of ascending aorta and aortic
arch

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Prognostic value of serum albumin in aortic
aneurysm patients undergoing graft
replacement of ascending aorta and aortic
arch

Directed by Professor Sung Yeon Ham

The Master's Thesis
submitted to the Department of Medicine,
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in partial fulfillment of the requirements for the degree of
Master of Medical Scienc

Won Seok Nam

December 2022

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ABSTRACT

Prognostic value of serum albumin in aortic aneurysm patients undergoing graft replacement of ascending aorta and aortic arch

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Background: Hypoalbuminemia is a marker of poor overall health with influences from protein energy malnutrition, systemic inflammation and hepatic and renal disease. Albumin has been reported to have a prognostic impact in various cohorts. This study investigated whether preoperative serum albumin level could be used for predicting mortality in aortic aneurysm patients undergoing graft replacement of ascending aorta and aortic arch.

Methods: We retrospectively reviewed 183 patients who underwent graft replacement of ascending aorta and aortic arch between January 2010 and December 2020. Patients were divided into two groups based on cut-off value obtained from combined receiver-operating characteristic curve analysis. Lower albumin group was defined as serum albumin <4.0 g/dL. The incidence of mortality was compared between the two groups, and logistic regression analysis was performed to evaluate the predictors for mortality.

Results: The optimal cut-off value of albumin to predict 1-year mortality was 4 g/dL (area under the curve 0.885, 95% CI 0.821–0.949, $p < 0.001$), with a sensitivity and specificity of 90.0% and 80.3%, respectively. The incidence of 1-year mortality was higher in the lower albumin group than the normal albumin group (0.7% vs. 20.9%, $p < 0.001$). Preoperative

serum albumin levels (OR = 0.116, 95% CI 0.021-0.641, p=0.014) and diabetes mellitus (OR = 5.757, 95% CI 1.018-32.565, p=0.048) remained as independent predictors of 1-year mortality.

Conclusion: Preoperative serum albumin level was an independent predictor of 1-year mortality after surgical repair of aortic aneurysm. Optimization of patients' nutritional status before surgery may be warranted and should be further explored in this high risk population.

Key words : Hypoalbuminemia, prognosis, aortic aneurysm, graft replacement, mortality

Prognostic value of serum albumin in aortic aneurysm patients undergoing graft replacement of ascending aorta and aortic arch

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I. INTRODUCTION

Patients undergoing graft replacement of ascending aorta and aortic arch are at high risk for poor clinical outcomes due to the nature of the disease, ischemia-reperfusion injury due to cardiopulmonary bypass, and inflammatory response.¹ A graft repair is the gold standard for treating aortic aneurysms, but the mortality rate is 3%, even in high-volume centers.² Therefore, several studies have been conducted to identify the prognostic factors for aortic aneurysms. Hypertension, atherosclerosis, dyslipidemia, and smoking have been identified as risk factors.³⁻⁵

Hypoalbuminemia has been reported to be a prognostic marker for malnutrition, systemic inflammation, and hepatic and renal diseases.⁶ Previous studies have shown that serum albumin is a prognostic marker for mortality and morbidity among patients with cardiovascular diseases, those receiving transplants, and those undergoing cardiac/non-cardiac surgeries.⁶⁻⁹

Aortic aneurysms develop through a process called cystic medial degeneration, which is also associated with connective tissue disorders such as Marfan syndrome and Ehlers-

Danlos syndrome. In previous studies on the sporadic forms of aortic aneurysms, inflammatory and immune cells infiltrated the aortic wall, suggesting that the inflammatory pathway may be critical in the development of aortic aneurysms.¹⁰ Since the inflammatory response plays an important role in the development of aortic aneurysms and nutrition and systemic inflammation play an important role in the prognosis of patients, several studies have been conducted to elucidate the role of albumin as a prognostic factor in these patients. Hypoalbuminemia is associated with poor clinical outcomes in abdominal aortic aneurysm repair and acute aortic dissection.^{11,12} However, the prognostic association between patients undergoing graft replacement of ascending aorta and aortic arch and preoperative serum albumin levels has not been fully described.

Therefore, this study aimed to examine whether serum albumin levels could be a prognostic marker of mortality and morbidity in patients undergoing graft replacement of ascending aorta and aortic arch.

II. MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Yonsei University Health System, Seoul, Korea (IRB No.3-2022-0367), and the need for informed consent from the patients was waived. All methods and procedures were performed in accordance with the relevant guidelines and regulations. This study was performed in accordance with the tenets of the Declaration of Helsinki.

1. Study population

We identified all patients who underwent graft replacement of ascending aorta and aortic arch between January 2010 and December 2020 at the Gangnam Severance Hospital, Yonsei University College of Medicine. Patients with traumatic aortic injuries (n=2), previous aortic repair within 6 months (n=2), ruptured aortic aneurysms (n=14), or a lack of preoperative laboratory data or medical records (n=10) were excluded. A total of 183

patients were included and analyzed in this study (Figure 1). The patients were divided into two groups based on cut-off value obtained from receiver-operating characteristic (ROC) curve analysis: lower (serum albumin < 4.0 g/dL) and higher (serum albumin \geq 4.0 g/dL) (Figure 2).

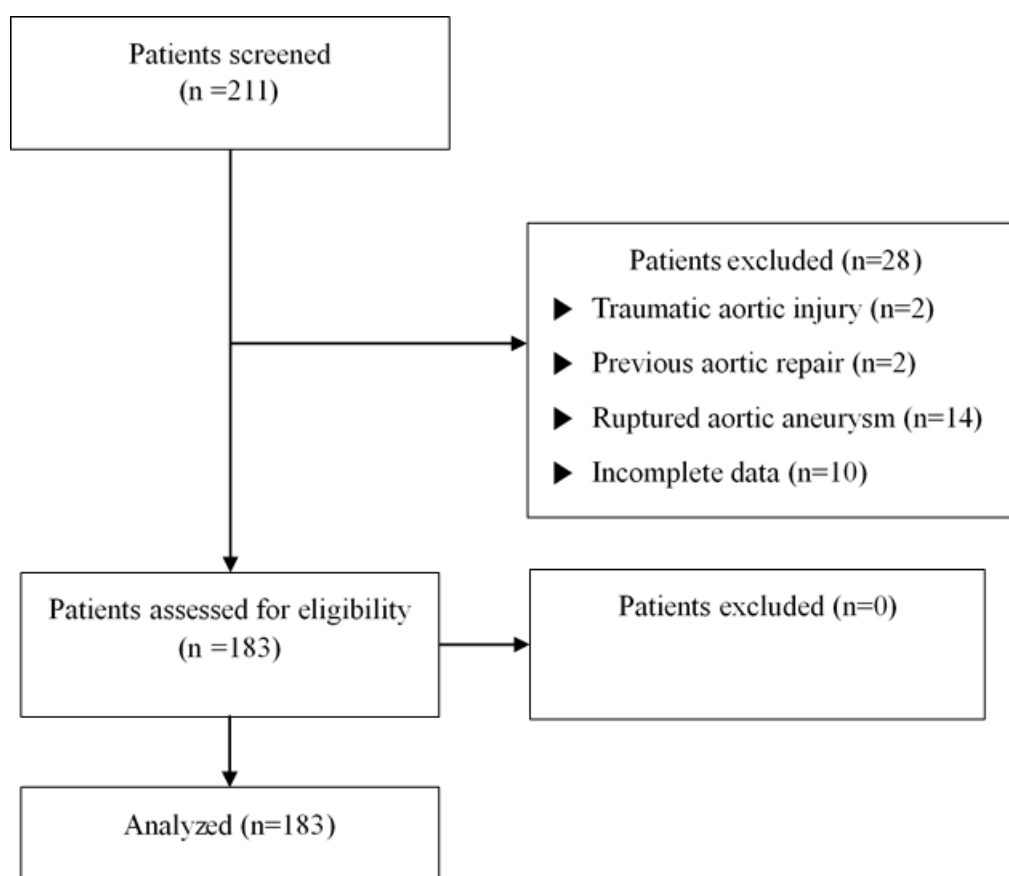


Figure 1. Flowchart of study enrolment

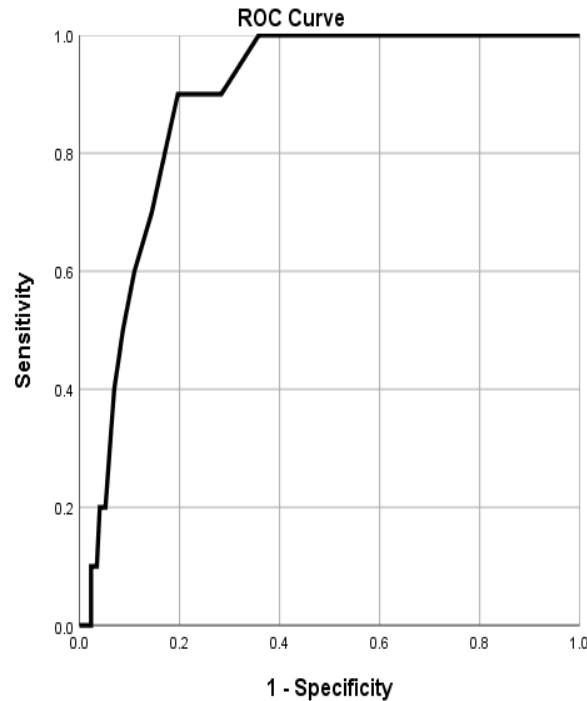


Fig 2. Combined receiver-operating characteristic curve of preoperative albumin levels for the incidence of 1-year mortality. The area under the curve = 0.885 and p -value <0.001 are observed below the line showing the serum albumin level with a 95% confidence interval of 0.821–0.949.

2. Demographic and Clinical Data

Demographic data included age, sex, height, weight, and current smoking status. Data on medical comorbidities such as hypertension, diabetes mellitus, acute/chronic renal failure, cerebrovascular accident/transient ischemic attack, coronary artery occlusive disease/coronary intervention history, and chronic obstructive pulmonary disease and medication (beta-blockers, calcium channel blockers, diuretics, angiotensin receptor blockers) for the mentioned diseases were collected. Perioperative laboratory data (1 month

prior to surgery to 1 year postoperatively) included CBC and routine chemistry (serum albumin, CRP, BUN/Cr, eGFR, OT/PT etc.). Postoperative outcomes included postoperative 1-year mortality and morbidities (mechanical ventilation > 24 h, reintubation, wound infection, pulmonary complication, myocardial infarction, arrhythmia, cerebrovascular accident, re-operation, acute kidney injury, use of CRRT). The definition of acute kidney injury was based on the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines.

3. Study endpoints

The primary endpoint of this study was to determine the prognostic value of preoperative serum albumin levels for predicting mortality in patients undergoing graft replacement of the ascending aorta and total arch. The secondary endpoints of this study were postoperative complications, comorbidities (mechanical ventilation > 24 h, reintubation, wound infection, pulmonary complication, myocardial infarction, arrhythmia, cerebrovascular accident, re-operation, acute kidney injury, and use of CRRT), length of hospital stay, and intensive care unit (ICU) stay.

4. Statistical analysis

Continuous variables are presented as mean \pm standard deviation for normally distributed data, or as medians (interquartile ranges) for skewed data. Normality was assessed using the Kolmogorov-Smirnov test. The independent t-test or Mann-Whitney U test was used to compare continuous variables. Categorical variables are described using absolute and relative (percentage) frequencies. Categorical variables were compared using the chi-squared or Fisher's exact test. We performed a logistic regression analysis to determine the predictors of 1-year mortality. For multivariate analysis, we used a stepwise selection method and selected variables with $p < 0.05$ in the univariate analysis. Predictability was expressed as odds ratios (OR) and 95% confidence intervals (CI). Receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of the

preoperative serum albumin level showing the best discriminatory capacity to predict postoperative 1-year mortality. Statistical significance was set at $p < 0.05$. The analysis was performed using SPSS version 23 (IBM Corp., Armonk, NY, USA).

III. RESULTS

A total of 211 patients were reviewed during the study period, and 183 patients were analyzed (Figure 1). The ROC curve of preoperative serum albumin levels for predicting 1-year mortality after total arch replacement demonstrated an area under the curve of 0.885. (95% CI 0.821–0.949, $p < 0.001$). The optimal cut-off value of albumin that predicted the incidence of 1-year mortality was 4.0 g/dL, with a sensitivity and specificity of 90.0% and 80.3%, respectively (Figure 2). Patients in the lower albumin group were significantly older than those in the higher albumin group (57.52 ± 15.40 vs. 68.33 ± 11.99 , $p < 0.001$). There was a higher prevalence of hypertension (54.3% vs. 79.1%, $p = 0.004$) and diuretic use (16.4% vs. 34.9%, $p = 0.009$) in the lower albumin group than in the higher albumin group. Preoperative laboratory data including total protein (7.22 ± 0.43 g/dL vs. 6.39 ± 0.68 g/dL, $p < 0.001$), hemoglobin (14.01 ± 1.62 g/dL vs. 11.93 ± 2.19 g/dL, $p < 0.001$), and hematocrit (41.69 ± 4.47 g/dL vs. 35.55 ± 6.19 g/dL, $p < 0.001$) were significantly lower in the lower albumin group than in the higher albumin group. White blood cell (WBC) count ($6.90 \pm 1.87 \times 10^3/\mu\text{L}$ vs. $8.38 \pm 3.99 \times 10^3/\mu\text{L}$, $p = 0.022$), CRP (4.09 ± 12.59 mg/L vs. 29.14 ± 44.93 mg/L, $p = 0.002$), and PT (1.01 ± 0.09 sec vs. 1.13 ± 0.36 sec, $p = 0.033$) were significantly higher in the lower albumin group than in the higher albumin group. The frequency of emergent repair was also higher in the lower albumin group than in the higher albumin group (14.3% vs. 28.6%, $p = 0.040$). The lower albumin group needed a shorter aorta cross-clamping time (98.36 ± 59.40 min vs. 78.62 ± 50.48 min, $p = 0.036$) and required more transfusion of packed red blood cells (1.17 ± 1.50 pack vs. 2.65 ± 2.34 pack, $p < 0.001$) (Table 1).

Table 1. Baseline characteristics and perioperative data of patients with aortic aneurysms presenting two comparative two preoperative albumin levels

	Higher albumin (n=140)	Lower albumin (n=43)	p-value
Demographics			
Female sex	38 (27.1%)	16 (37.2%)	0.206
Age (years)	57.52±15.40	68.33±11.99	<0.001*
Body mass index (kg/m ²)	23.97±3.49	22.94±3.63	0.099
Comorbidities			
Smoking	64 (46.0%)	19 (44.2%)	0.831
Hypertension	76 (54.3%)	34 (79.1%)	0.004*
Diabetes mellitus	11 (7.9%)	6 (14.0%)	0.237
CAOD	12 (8.6%)	4 (9.3%)	1.000
COPD	3 (2.1%)	1 (2.3%)	1.000
CVA	8 (5.7%)	4 (9.3%)	0.480
ARF	0	1 (2.3%)	0.235
CRF	5 (3.6%)	4 (9.3%)	0.218
Medications			
β-blockers	41 (29.3%)	18 (41.9%)	0.123
CCB	49 (35.0%)	14 (32.6%)	0.768
ARB	63 (45.0%)	22 (51.2%)	0.478
Statin	46 (32.9%)	13 (30.2%)	0.747
Diuretics	23 (16.4%)	15 (34.9%)	0.009*
Preoperative laboratory data			
ALP (IU/L)	80.72±28.82	86.68±46.94	0.447
AST (IU/L)	24.93±7.62	99.33±306.40	0.151
ALT (IU/L)	22.79±13.07	62.26±147.02	0.086

BUN (mg/dL)	17.01±5.75	21.48±11.46	0.017*
Creatinine (mg/dL)	0.90±0.38	1.39±1.71	0.066
Total bilirubin (mg/dL)	0.78±0.39	0.81±0.59	0.750
Total protein (g/dL)	7.22±0.43	6.39±0.68	<0.001*
Hemoglobin (g/dL)	14.01±1.62	11.93±2.19	<0.001*
Hematocrit (%)	41.69±4.47	35.55±6.19	<0.001*
WBC (10 ³ /μL)	6.90±1.87	8.38±3.99	0.022*
Platelet (10 ³ /μL)	231.37±59.27	222.40±99.77	0.578
Prothrombin time (sec)	1.01±0.09	1.13±0.36	0.033*
C-reactive protein (mg/L)	4.09±12.59	29.14±44.93	0.002*
Operative data			
Emergency	20 (14.3%)	12 (28.6%)	0.040*
Anesthesia time (min)	400.79±86.72	383.49±72.14	0.237
Operative time (min)	307.02±90.97	290.64±75.36	0.290
CPB time (min)	168.54±55.70	154.45±43.63	0.143
ACC time (min)	98.36±59.40	78.62±50.48	0.036*
TCA time (min)	25.99±22.08	33.49±22.19	0.054
pRBC transfusion (pack)	1.17±1.50	2.65±2.34	<0.001*
FFP transfusion (pack)	4.46±1.51	4.53±1.26	0.781
Platelet transfusion (pack)	11.99±4.76	11.05±5.16	0.269

Values are presented as mean ± standard deviation or number of patients (%).

CAOD, coronary artery occlusive disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident, ARF, acute renal failure; CRF, chronic renal failure; CCB, calcium channel blocker; ARB, angiotensin receptor blocker; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; WBC, white blood cells; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; TCA, total circulatory arrest; pRBC: packed red blood cell; FFP, fresh frozen plasma; * $p < 0.05$.

Table 2 summarizes the incidences of postoperative morbidity and mortality. The incidence of mechanical ventilation requiring more than 24 h was higher in the lower albumin group than in the higher albumin group (11.4% vs. 27.9%, $p=0.009$). The postoperative need for continuous renal replacement therapy was also more common in the lower albumin group than in the higher albumin group (0.7% vs. 23.3%, $p<0.001$). A greater proportion of patients in the lower albumin group had pulmonary complications than those in the higher albumin group (5.0% vs. 18.6%, $p=0.009$). Moreover, the incidence of 1-year mortality was significantly higher in the lower albumin group than in the higher albumin group (0.7% vs. 20.9%, $p<0.001$) (Table 2).

Table 2. Postoperative morbidity and mortality of patients with aortic aneurysms presenting two comparative preoperative albumin levels.

	Higher albumin (n=140)	Lower albumin (n=43)	p-value
Hospital day (day)	20.21±28.98	29.72±25.03	0.054
TND	3 (2.1%)	1 (2.3%)	1.000
CVA	7 (5.0%)	4 (9.3%)	0.289
Reintubation	4 (2.9%)	4 (9.3%)	0.089
MV>24 hrs	16 (11.4%)	12 (27.9%)	0.009*
RRT	1 (0.7%)	10 (23.3%)	<0.001*
AKI	13 (9.3%)	8 (18.6%)	0.105
Infection	16 (11.4%)	10 (23.3%)	0.052
Pulmonary Cx	7 (5.0%)	8 (18.6%)	0.009*
MI	0	2 (4.7%)	0.054
Arrhythmia	14 (10.0%)	8 (18.6%)	0.129
Reoperation	4 (2.9%)	2 (4.7%)	0.627

ICU readmission	8 (5.7%)	6 (14.0%)	0.099
30-d mortality	0	2 (4.7%)	0.054
1-y mortality	1 (0.7%)	9 (20.9%)	<0.001*

Values are presented as mean \pm standard deviation or number of patients (%).

TND, transient neurological deficit; CVA, cerebrovascular accident; MV, mechanical ventilation; RRT, renal replacement therapy; AKI, acute kidney injury; Pulmonary Cx, pulmonary complication; MI, myocardial infarction; ICU, intensive care unit; * $p < 0.05$.

Logistic regression analysis showed that age, diabetes mellitus, preoperative hemoglobin, and the preoperative serum albumin level showed a difference with $p < 0.05$ for predicting 1-year mortality of patients. Preoperative serum albumin levels (OR = 0.116, 95% CI 0.021-0.641, $p = 0.014$) and diabetes mellitus (OR = 5.757, 95% CI 1.018-32.565, $p = 0.048$) remained as independent predictors of 1-year mortality in the multivariate analysis (Table 3).

Table 3. Logistic regression analysis for predictors of 1-year mortality of patients after graft replacement of ascending aorta and aortic arch.

	Univariate OR (CI)	P-value	Multivariate OR (CI)	P-value
Age	1.104 (1.021-1.193)	0.013	1.108 (0.998-1.230)	0.054
Smoking	0.785 (0.214-2.880)	0.715		
Hypertension	2.784 (0.574-13.502)	0.204		
Diabetes mellitus	4.867 (1.132-20.931)	0.033	5.757 (1.018-32.565)	0.048*
CAOD	2.839 (0.549-14.681)	0.213		
CRF	2.292 (0.258-20.363)	0.457		
Emergency	3.429 (0.908-12.942)	0.069		
Reoperation	3.733 (0.394-35.397)	0.251		
Preop Hb	0.634 (0.459-0.876)	0.006	1.050 (0.674-1.636)	0.829

Albumin	0.105 (0.013-0.350)	<0.001	0.116 (0.021-0.641)	0.014*
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Values are presented as odds ratio (95% confidential interval).

CAOD, Coronary artery occlusive disease; CRF, Chronic renal failure; Preop, preoperative; Hb, hemoglobin; * $p < 0.05$.

Table 4 shows the baseline characteristics and outcome variables of the patients stratified according to 1-year mortality. Non-survivors showed significantly lower preoperative serum albumin levels than survivors (4.23 ± 0.45 g/dL vs. 3.59 ± 0.37 g/dL, $p < 0.001$) (Table 4).

Table 4. Baseline characteristics and laboratory data of patients with aortic aneurysms, stratified according to 1-year mortality.

	Survivor (n=173)	Non-survivor (n=10)	p-value
Demographics			
Female sex	53 (30.6%)	1 (10.0%)	0.285
Age (years)	59.32 ± 15.40	72.90 ± 5.65	<0.001*
Body mass index (kg/m ²)	23.79 ± 3.47	22.76 ± 4.69	0.372
Comorbidities			
Smoking	79 (45.9%)	4 (40.0%)	0.757
Hypertension	102 (59.0%)	8 (80.0%)	0.320
Diabetes mellitus	14 (8.1%)	3 (30.0%)	0.053
CAOD	14 (8.1%)	2 (20.0%)	0.213
COPD	4 (2.3%)	0	1.000
CVA	12 (6.9%)	0	1.000
ARF	1 (0.6%)	0	1.000
CRF	8 (4.6%)	1 (10.0%)	0.404
Preoperative laboratory data			
Albumin (g/dL)	4.23 ± 0.45	3.59 ± 0.37	<0.001*

ALP (IU/L)	81.90±33.57	86.60±43.09	0.673
AST (IU/L)	35.73±142.52	132.10±241.17	0.241
ALT (IU/L)	27.17±55.87	116.80±202.75	0.196
BUN (mg/dL)	17.69±7.36	24.43±10.69	0.079
Creatinine (mg/dL)	1.00±0.91	1.31±0.87	0.288
Total bilirubin (mg/dL)	0.76±0.41	1.16±0.79	0.149
Total protein (g/dL)	7.06±0.59	6.49±0.77	0.004*
Hemoglobin (g/dL)	13.62±1.92	11.74±2.19	0.003*
Hematocrit (%)	40.57±5.39	34.71±5.76	0.001*
C-reactive protein (mg/L)	8.64±22.27	43.38±62.32	0.113

Values are presented as the mean ± standard deviation or number of patients (%).

CAOD, Coronary artery occlusive disease; COPD, Chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ARF, acute renal failure; CRF, chronic renal failure; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; * $p < 0.05$.

IV. DISCUSSION

In this retrospective study, we investigated the association between preoperative serum albumin levels and postoperative 1-year mortality in patients undergoing graft replacement of ascending aorta and aortic arch. Preoperative serum albumin level was an independent predictor of 1-year mortality along with diabetes mellitus.

Albumin is a negative acute-phase reactant and its level decreases during injuries and sepsis. Albumin has been reported to be a marker of nutrition and is involved in many biological functions, such as the regulation of oncotic pressure, transport of compounds, and antioxidant activity.¹³ Albumin is a well-known marker of nutritional status and has been shown to be related to prognosis. Albumin is a valuable marker of in-hospital malnutrition and frailty.¹⁴ An inadequate nutritional status, indicated by low albumin levels,

can lead to poor inflammatory and immune responses to surgery. Hypoalbuminemia has been demonstrated to be associated with postoperative mortality in cardiac and non-cardiac surgeries.^{6,8,11,12,15} A previous study conducted in patients with abdominal aortic aneurysms reported that preoperative hypoalbuminemia was associated with increased mortality, longer length of hospital stay, pulmonary complications, and reoperations.¹¹ Hypoalbuminemia was an independent predictor of mortality in patients with type A and B acute aortic dissection.¹² Serum albumin levels lower than 2.5 g/dL were an independent predictor of mortality and morbidity in patients undergoing cardiac surgery using cardiopulmonary bypass.¹⁵ In accordance with the literature, hypoalbuminemia was an independent predictor of 1-year mortality in patients who underwent graft replacement of ascending aorta and aortic arch in the present study.

Albumin is involved in the regulation of oncotic pressure, which is closely associated with microvascular permeability. When capillary endothelial cells are injured by inflammatory cytokines, vascular leakage occurs, leading to hypoalbuminemia.¹⁶ Furthermore, vascular endothelial dysfunction is closely associated with hypertension pathogenesis.¹⁷ The higher incidence of hypertension in the lower albumin group in our study suggests an association between hypertension, vascular permeability, and hypoalbuminemia; however, this is beyond the scope of this study.

The inflammatory pathway is critical for the development of aortic aneurysms.^{10,18} T-cell and macrophage infiltrations are present in aortic aneurysms.¹⁹ Albumin is a well-known negative acute-phase reactant that is reported to decrease during injury and sepsis. Additionally, albumin has an anti-inflammatory effect that can counteract the mechanism of aortic aneurysm formation.^{10,20} Another plausible explanation can be the oxidative stress involved in the pathophysiology of aortic aneurysms.^{10,18} Thoracic aortic tissues from patients with Marfan syndrome have shown increased levels of oxidative stress.²¹ Albumin has also been shown to be involved in extracellular antioxidant defenses.¹³ Albumin levels not only decrease in response to inflammation but albumin also has anti-inflammatory and

antioxidant effects; therefore, a decrease in albumin levels leads to a decrease in this protective action.

Serum albumin levels are known to be decreased in older patients.^{22,23} Similarly, the lower albumin group was significantly older than the higher albumin group in the current study. This age-related decline in albumin levels may be related to frailty and nutritional status. As old age is known to be a predictor of mortality and morbidity in several patient groups undergoing surgery, the influence of age on albumin may have contributed to its role as a predictor of mortality in this study.^{24,25}

In our study the ROC curve analysis showed an optimal cut-off value of 4.0, which is higher than that reported in previous studies. A previous study evaluating hypoalbuminemia, mortality, and morbidity in patients undergoing left ventricular device implantation stated that serum albumin < 2.5 g/dL is a risk factor for mortality and morbidity.²⁶ Another study of patients with acute aortic dissection also showed albumin < 3.4 g/dL as a prognostic factor for mortality.¹² Other studies reported that serum albumin < 2.5 g/dL is associated with increased mortality and morbidity in cardiac surgeries, including coronary bypass operations or valve surgeries.¹⁵ The higher cut-off value in our study needs further evaluation, but the exclusion of ruptured aneurysm and aortic dissection patients, a relatively younger study population, and a relatively small study sample may have influenced the higher cut-off value. However, our study is among the first to show the cut-off value of serum albumin in patients undergoing graft replacement of ascending aorta and aortic arch.

This study extends prior work by investigating the effects of preoperative albumin levels on patients who underwent graft replacement of ascending aorta and aortic arch, denoting that intervention in the preoperative nutritional status of aortic aneurysm patients may lead to better postoperative outcomes.

This study has some limitations. Firstly, this was a retrospective study, in which inherent biases of confounding and selection existed. Secondly, this was a single-center study that evaluated 183 patients, which is a relatively small sample and the incidence of mortality

was not high enough to provide statistical evidence. Lastly, our analysis had limitations in capturing factors that could cause lower serum albumin levels, such as autoimmune and liver diseases.

V. CONCLUSION

Lower serum albumin levels are associated with higher mortality and morbidity in patients undergoing graft replacement of ascending aorta and aortic arch. This denotes the necessity to routinely measure serum albumin levels before surgery and that the optimization of patients' nutritional status before surgery may be warranted and should be further explored in high-risk patients.

REFERENCES

1. Ailawadi G, Zacour RK. Cardiopulmonary bypass/extracorporeal membrane oxygenation/left heart bypass: indications, techniques, and complications. *Surg Clin North Am* 2009;89:781-96, vii-viii.
2. Tan G, Khoo P, Chan K. A review of endovascular treatment of thoracic aorta disease. *Ann R Coll Surg Engl* 2018;100:1-6.
3. Senser EM, Misra S, Henkin S. Thoracic Aortic Aneurysm: A Clinical Review. *Cardiol Clin* 2021;39:505-15.
4. Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. *Nat Clin Pract Cardiovasc Med* 2007;4:418-27.
5. Boodhwani M, Andelfinger G, Leipsic J, Lindsay T, McMurtry MS, Therrien J, et al. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. *Can J Cardiol* 2014;30:577-89.
6. Baldwin MR, Arcasoy SM, Shah A, Schulze PC, Sze J, Sonett JR, et al. Hypoalbuminemia and early mortality after lung transplantation: a cohort study. *Am J Transplant* 2012;12:1256-67.
7. Bonilla-Palomas JL, Gámez-López AL, Moreno-Conde M, López-Ibáñez MC, Anguita-Sánchez M, Gallego de la Sacristana A, et al. Hypoalbuminemia in acute heart failure patients: causes and its impact on hospital and long-term mortality. *J Card Fail* 2014;20:350-8.
8. Chahrour MA, Kharroubi H, Al Tannir AH, Assi S, Habib JR, Hoballah JJ. Hypoalbuminemia is Associated with Mortality in Patients Undergoing Lower Extremity Amputation. *Ann Vasc Surg* 2021;77:138-45.
9. Doucette K, Percival ME, Williams L, Kandahari A, Taylor A, Wang S, et al. Hypoalbuminemia as a prognostic biomarker for higher mortality and treatment complications in acute myeloid leukemia. *Hematol Oncol* 2021;39:697-706.

10. El-Hamamsy I, Yacoub MH. Cellular and molecular mechanisms of thoracic aortic aneurysms. *Nat Rev Cardiol* 2009;6:771-86.
11. Inagaki E, Farber A, Eslami MH, Kalish J, Rybin DV, Doros G, et al. Preoperative hypoalbuminemia is associated with poor clinical outcomes after open and endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2017;66:53-63.e1.
12. Gao Y, Li D, Cao Y, Zhu X, Zeng Z, Tang L. Prognostic value of serum albumin for patients with acute aortic dissection: A retrospective cohort study. *Medicine (Baltimore)* 2019;98:e14486.
13. Sitar ME, Aydin S, Cakatay U. Human serum albumin and its relation with oxidative stress. *Clin Lab* 2013;59:945-52.
14. Moramarco S, Morciano L, Morucci L, Messinese M, Gualtieri P, Carestia M, et al. Epidemiology of Hypoalbuminemia in Hospitalized Patients: A Clinical Matter or an Emerging Public Health Problem? *Nutrients* 2020;12.
15. Engelman DT, Adams DH, Byrne JG, Aranki SF, Collins JJ, Jr., Couper GS, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg* 1999;118:866-73.
16. Böhm M, Thoenes M, Danchin N, Bramlage P, La Puerta P, Volpe M. Association of cardiovascular risk factors with microalbuminuria in hypertensive individuals: the i-SEARCH global study. *J Hypertens* 2007;25:2317-24.
17. Dinh QN, Drummond GR, Sobey CG, Chrissobolis S. Roles of inflammation, oxidative stress, and vascular dysfunction in hypertension. *Biomed Res Int* 2014;2014:406960.
18. Quintana RA, Taylor WR. Cellular Mechanisms of Aortic Aneurysm Formation. *Circ Res* 2019;124:607-18.
19. He R, Guo DC, Sun W, Papke CL, Duraisamy S, Estrera AL, et al. Characterization of the inflammatory cells in ascending thoracic aortic aneurysms in patients with Marfan syndrome, familial thoracic aortic aneurysms, and sporadic aneurysms. *J Thorac Cardiovasc Surg* 2008;136:922-9, 9.e1.

20. Wiedermann CJ. Anti-inflammatory activity of albumin. *Crit Care Med* 2007;35:981-2; author reply 2-3.
21. Yang HH, van Breemen C, Chung AW. Vasomotor dysfunction in the thoracic aorta of Marfan syndrome is associated with accumulation of oxidative stress. *Vascul Pharmacol* 2010;52:37-45.
22. Salive ME, Cornoni-Huntley J, Phillips CL, Guralnik JM, Cohen HJ, Ostfeld AM, et al. Serum albumin in older persons: relationship with age and health status. *J Clin Epidemiol* 1992;45:213-21.
23. Greenblatt DJ. Reduced serum albumin concentration in the elderly: a report from the Boston Collaborative Drug Surveillance Program. *J Am Geriatr Soc* 1979;27:20-2.
24. Guo MH, Tran D, Ahmadvand A, Coutinho T, Glineur D, Al-Atassi T, et al. Perioperative and Long-Term Morbidity and Mortality for Elderly Patients Undergoing Thoracic Aortic Surgery. *Semin Thorac Cardiovasc Surg* 2020;32:644-52.
25. Mahdi H, Wiechert A, Lockhart D, Rose PG. Impact of Age on 30-Day Mortality and Morbidity in Patients Undergoing Surgery for Ovarian Cancer. *Int J Gynecol Cancer* 2015;25:1216-23.
26. Go PH, Hodari A, Nemeh HW, Borgi J, Lanfear DE, Williams CT, et al. Effect of Preoperative Albumin Levels on Outcomes in Patients Undergoing Left Ventricular Device Implantation. *Asaio j* 2015;61:734-7.

ABSTRACT(IN KOREAN)

상행 대동맥과 대동맥궁 치환술을 시행 받는 대동맥류 환자에서 혈청
알부민의 예후 예측 인자로써의 역할

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남원석

연구배경: 저알부민혈증은 전반적인 건강상태의 악화, 단백질 에너지 영양실조, 전신적인 염증, 신장 및 간질환의 지표이다. 알부민은 다양한 연구에서 예후를 예측하는 인자임이 밝혀졌다. 본 연구는 수술전 혈청알부민이 상행 대동맥과 대동맥궁 치환술을 받는 대동맥류환자에서 사망률을 예측할 수 있는지 알아보려고 한다.

연구방법: 본 연구는 후향적 연구로 2010 년 1 월부터 2020 년 12 월까지 상행 대동맥과 대동맥궁 치환술을 받은 184 명의 환자를 대상으로 하였다. 환자들은 Receiver operating characteristic curve analysis 에 따라 두 그룹으로 분류되었다. 저알부민 그룹은 혈청알부민이 4.0g/dL 미만인 환자들로 정의하였다. 이 연구에서는 두 그룹의 사망률을 비교하고 다중 로지스틱 회귀분석을 통해 사망을 예측할 수 있는 예후 인자를 살펴보았다.

Results: 수술 후 1 년 사망률을 예측하는 혈청 알부민의 최적 절단치는 4g/dL (area under the curve 0.885, 95% CI 0.821–0.949, $p < 0.001$)였고, 민감도 90.0% 특이도 80.3% 이었다. 수술 후 1 년 사망률은 정상알부민 그룹보다 저알부민 그룹에서 유의미하게 높았다. (0.7% vs. 20.9%, $p < 0.001$). 수술 전 혈청알부민(odds ratio [OR] 0.116, 95% CI 0.021–0.641, $p = 0.014$)과 당뇨 (OR 5.757, 95% CI 1.018–32.565, $p = 0.048$)은 사망을 예측하는 독립적인 예후인자였다.

결론: 낮은 수술 전 혈청알부민 수치는 상행 대동맥과 대동맥 궁 치환술의 수술 후 1 년 사망률을 독립적으로 예측하는 예후인자였다. 따라서 고위험군인 환자에서 수술 전 영양상태를 관리하는 것이 중요하다고 볼 수 있다.

핵심되는 말: 저알부민혈증, 예후, 대동맥류, 대동맥과 대동맥궁 치환술 사망률