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ORIGINAL RESEARCH

Peripheral Eosinophil Count Is Associated With the Prognosis of Patients With Type B Aortic Dissection Undergoing Endovascular Aortic Repair: A Retrospective Cohort Study

Kaiwen Zhao, MD; Hongqiao Zhu, MD; Jiqing Ma, MD; Zhiqing Zhao, MD, PhD; Lei Zhang, MD; Zan Zeng, MD; Pengcheng Du, MD; Yudong Sun, MD; Qin Yang, MD; Jian Zhou, MD, PhD; Zaiping Jing, MD, PhD

BACKGROUND: Eosinophil count (EOS) has been proposed to provide prognostic information in multiple cardiovascular disorders. However, few researchers have investigated the predictive value of EOS for patients with type B aortic dissection who had thoracic endovascular repair.

METHODS AND RESULTS: The authors reviewed the records of 912 patients with type B aortic dissection who were treated with thoracic endovascular repair in Changhai Hospital, Shanghai. By using receiver operating characteristic curve analysis, patients were divided into 2 groups based on the admission EOS cutoff value (<7.4×10^6/L [n=505] and ≥7.4×10^6/L [n=407]). To reduce selection bias, propensity score matching was applied. Multivariable regression analysis and Kaplan–Meier curves were performed to assess the association between EOS and long-term outcomes. Furthermore, we investigated nonlinear correlations between EOS and outcomes using general additive models with restricted cubic splines. In the matched population, lower EOS was associated with significantly higher 30-day mortality (4.1% vs 0%, *P*=0.007). There was no statistically difference in 30-day adverse events between the 2 groups (all *P*>0.05). Kaplan–Meier analysis revealed that patients with an EOS <7.4×10^6/L had a higher incidence of 1-year all-cause death (7.95% vs. 2.34%, *P*=0.008) and aortic-related death (5.98% vs 1.81%, *P*=0.023) than those with higher EOS. Multivariable Cox analysis showed that continuous EOS was independently associated with 1-year mortality (hazard ratio, 3.23 [95% CI, 1.20–8.33], *P*=0.019). In addition, we discovered a nonlinear association between EOS and 1-year outcomes.

CONCLUSIONS: Lower admission EOS values predict higher short- and long-term mortality after thoracic endovascular repair.

Key Words: endovascular aortic repair ■ eosinophile count ■ prognosis ■ type B aortic dissection

Type B aortic dissection (TBAD) is a life-threatening disease, which is classified as any aortic dissection (AD) with an entry tear in zone 1 or a more distal aortic zone.[1] Recent clinical trials revealed that thoracic endovascular aortic repair (TEVAR), compared with optimal medical therapy, was linked with a lower risk of long-term mortality and fewer aortic-related adverse events (ARAEs) in patients with TBAD.[2,3] However, the potential complications associated with TEVAR limited its application.[4] In this context, identifying prognostic indicators would benefit risk stratification and improve the prognosis of patients with TBAD.

Correspondence to: Jian Zhou and Zaiping Jing, Department of Vascular Surgery, the First Affiliated Hospital of the Navy Medical University Shanghai, 200433 Shanghai, China. Email: zhoujian1-2@163.com; jingzaiping_vasc@163.com

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K. Zhao, H. Zhu, and J. Ma contributed equally as co-first authors.

J. Zhou and Z. Jing contributed equally to this article as co-senior authors.

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CLINICAL PERSPECTIVE

What Is New?

- Eosinophils play various roles in stress reaction, inflammation response, and coagulation.
- Eosinophil count is an independent predictor in patients with type B aortic dissection who had thoracic endovascular aortic repair.

What Are the Clinical Implications?

- Eosinophils are often overlooked in clinical practice, which may be a valuable prognostic indicator for a patient's perioperative stress response, inflammation, and coagulation, as well as postoperative prognosis risk.

Nonstandard Abbreviations and Acronyms

AD	aortic dissection
ARAE	aortic-related adverse event
EOS	eosinophil count
HPA	hypothalamic-pituitary-adrenal
PSM	propensity score matching
RTAD	retrograde type A aortic dissection
TBAD	type B aortic dissection
TEVAR	thoracic endovascular aortic repair

Several clinical laboratory markers, including C-reactive protein,[5] neutrophil/lymphocyte ratio,[6] and platelets,[7] have been reported to be linked to the mortality of patients with AD. Eosinopenia has been identified as a significant risk factor for poor clinical outcomes in patients with acute myocardial infarction.[8] Previous research has shown that eosinophil levels in patients with TBAD are much lower than in healthy patients,[9] and low eosinophil count (EOS) was correlated with a higher risk of all-cause death in patients with type A AD (TAAD) after surgery.[10] However, its value in the prediction of prognosis has not been reported for patients with TBAD.

The aim of the current study was to evaluate the prognostic value of EOS for patients with TBAD who received TEVAR.

METHODS

Study Population

The present study is based on a retrospective database, which is available from the corresponding author upon reasonable request. The research comprised 1416 consecutive patients with TBAD who underwent TEVAR at Changhai Hospital (Shanghai, China) from January 2003 to July 2019. The exclusion criteria included: (1) traumatic AD; (2) Marfan syndrome; (3) previous aortic surgery; (4) onset >90 days before treatment[11]; (5) history of glucocorticoid use; (6) eosinophilia, allergic rhinitis, bronchial asthma, or other history of allergic diseases; (7) and missing admission EOS measurement (Figure 1). The research protocol was authorized by the Shanghai Changhai Hospital's central ethics committee (CHEC-Y2020, March 1, 2020). Institutional review board approval was obtained according to the guidelines of *Journal of the American Heart Association* (*JAHA*). Informed consent was waived because of the retrospective nature of the study.

Data Collection and Definitions

Data from the records were retrieved on basic patient clinical findings, demographics, laboratory results, and the existence of comorbidity. An AD with an entry tear in zone 1 or a more distal aortic zone is classified as TBAD.[11] AD was classified as acute (1–14 days), subacute (15–90 days), and chronic (>90 days) according to guidelines published by the Society for Vascular Surgery/Society of Thoracic Surgeons.[11] Fasting blood samples of patients who received limited surgery were collected at 6 AM on the day of operation. If it was an emergency surgery, the blood samples were obtained in the emergency department or during surgery. An automated blood cell counter was used to count white blood cells (WBCs), platelets, and other blood cells (LH780, Beckman Coulter). Based on the receiver operating characteristic curve analysis, study participants were divided into 2 groups: the low EOS group ($<7.4\times10^6$/L [n=505]) and the high EOS group ($\geq7.4\times10^6$/L [n=407]).

Follow-Up and End Points

All patients were followed up by qualified researchers through phone survey or medical records. Furthermore, the comprehensive clinical files of readmitted patients and outpatients were examined for adverse events. The end points of this study were classified as short-term outcomes, which included 30-day all-cause death; 30-day stroke; 30-day organ failures; and 30-day ARAEs such as aortic rupture, malperfusion, retrograde type A dissection, dilation, and type I/III endoleak;[12] and long-term outcomes, including 1-year all-cause death and 1-year ARAEs.

Statistical Analysis

According to the distribution features, continuous variables were reported as mean (SD) or median (quartile 1–quartile 3) and compared using the Student *t* test or

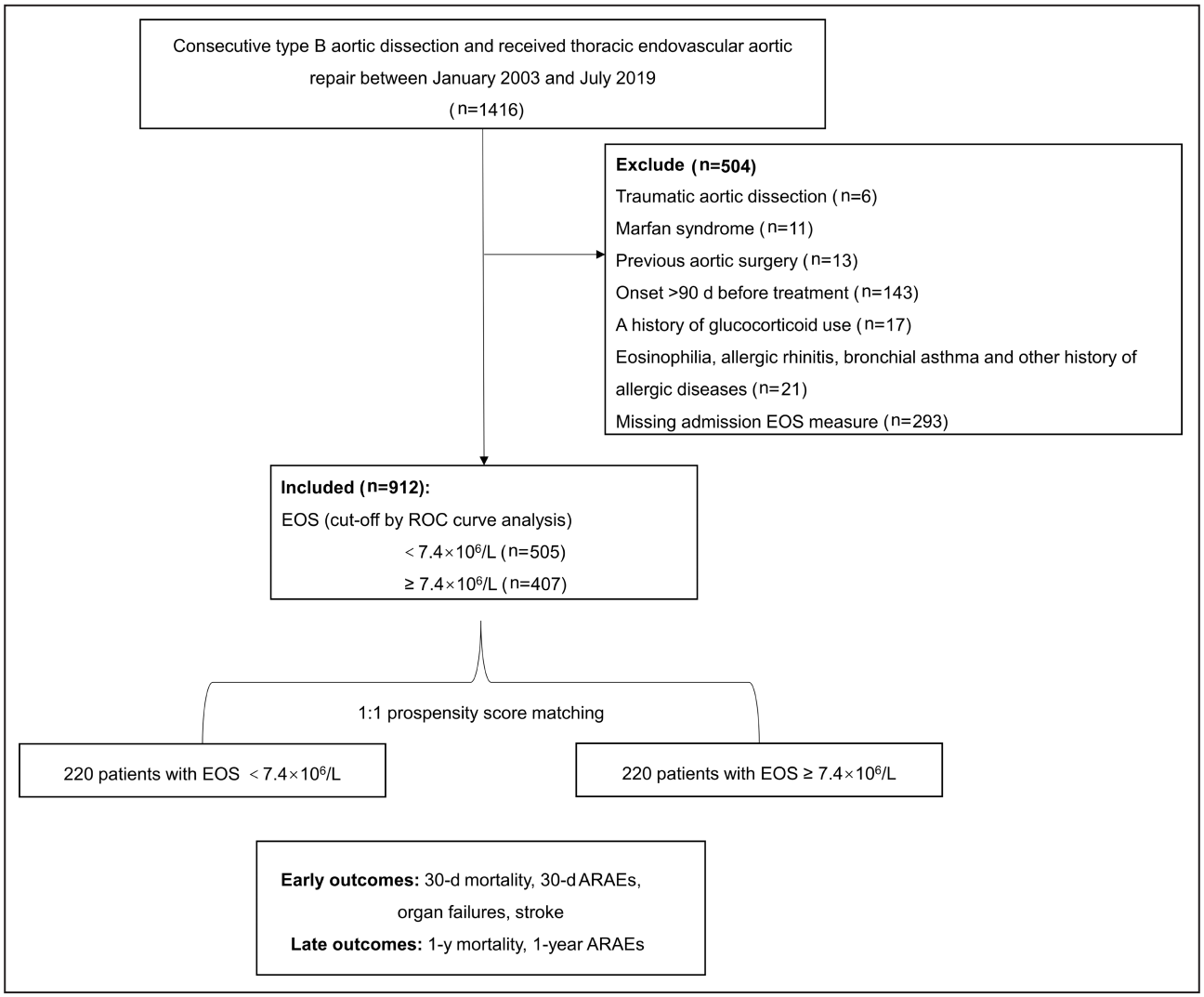

Figure 1. Flowchart of the patient selection process.
ARAEs indicates aortic-related adverse events; EOS, eosinophil count; and ROC, receiver operating characteristic.

Mann-Whitney test. Data for categorical variables were reported as percentages and tested using the χ^2 test or Fisher exact test. To assess the predictive validity of EOS for 30-day all-cause mortality, the receiver operating characteristic curve was established, and the area under the curve was compared using the Delong approach. EOS were originally input as a continuous variable and then modeled as a categorical variable, with the best cutoff determined using a receiver operating characteristic curve. The Kaplan-Meier method was used to compute cumulative survival curves, and log-rank tests were utilized to differentiate across group curves.

To compensate for baseline differences and reduce selection bias, a propensity score–matching (PSM) study was performed using a caliper of 0.05 and a 1:1 nearest-neighbor matching. Each patient's propensity score was determined using a logistic regression model and the characteristics are given in Table 1. The standardized mean difference was used to compare the differences among groups after PSM. A maximum standardized mean difference of 0.15 is often regarded as appropriate.[13]

To examine the relationship between preoperative EOS level and long-term outcomes, univariable and multivariable Cox regression models for 1-year all-cause mortality were conducted, as were Cox regression models for 1-year ARAEs. Using a forward stepwise technique, variables having a *P* value of <0.1 in the univariable analysis were added into the multivariable models before PSM. Those imbalanced variables after PSM (standardized mean difference >0.15) were adjusted considering the clustering on the matched pairs. The proportional hazard assumption of Cox models was evaluated and no covariates in adjusted models were time-dependent variables

Table 1. Baseline Characteristics, Anatomical Characteristics, and Intraoperative Details Stratified by Preoperative EOS Counts Before and After PSM

Variables	Unmatched groups				Propensity score–matched groups			
	Low EOS (n=505)	High EOS (n=407)	SMD	*P* value	Low EOS (n=220)	High EOS (n=220)	SMD	*P* value
Baseline characteristics								
Age, y	59.1±13.0	57.8±13.2	0.100	0.133	59.7±12.7	58.6±13.3	0.081	0.396
Men	412 (81.6)	354 (87.0)	0.149	0.027	185 (84.1)	184 (83.6)	0.012	1.0
BMI	24.4±3.5	24.7±3.8	0.072	0.337	24.3±3.3	24.4±3.8	0.049	0.607
Smoking	275 (54.5)	278 (68.3)	0.525	<0.001	128 (58.2)	133 (60.3)	0.073	0.550
SBP at admission, mm Hg	140.5±23.0	136.1±19.4	0.207	0.002	137.5±19.5	136.3±20.1	0.061	0.524
DBP at admission, mm Hg	83.2±12.3	82.2±10.7	0.092	0.17	82.2±10.7	82.1±10.6	0.002	0.986
WBC, $\times 10^9$/L	9.5±4.2	8.4±2.9	0.309	<0.001	8.9±3.8	8.5±3.3	0.119	0.213
Hemoglobin, g/L	127.2±19.5	129.7±19.8	0.124	0.041	129.0±20.5	129.1±20.9	0.004	0.969
Creatinine, μmol/L	102.5±116.7	106.8±103.6	0.039	0.576	107.8±135.9	109.1±116.5	0.011	0.908
Platelet, $\times 10^9$/L	187.3±72.1	239.5±96.3	0.613	<0.001	206.8±4.5	219.0±78.6	0.160	0.094
Comorbidities								
Hypertension	378 (74.9)	313 (76.9)	0.048	0.472	165 (75)	165 (75)	<0.001	1.0
Diabetes	33 (6.5)	46 (11.3)	0.168	0.011	22 (10)	17 (7.7)	0.08	0.502
Stroke	27 (5.4)	28 (6.9)	0.064	0.334	14 (6.4)	12 (5.5)	0.039	0.840
COPD	53 (10.5)	48 (11.8)	0.041	0.534	26 (11.8)	24 (10.9)	0.029	0.881
CKD	28 (5.5)	25 (6.1)	0.025	0.701	14 (6.4)	16 (7.3)	0.036	0.850
CAD	26 (5.2)	20 (4.9)	0.011	0.872	11 (5)	10 (4.5)	0.021	1.0
Pericardial effusion	37 (7.3)	25 (6.1)	0.047	0.480	10 (4.5)	13 (5.9)	0.061	0.668
Pleural effusion	185 (36.6)	139 (34.2)	0.052	0.436	78 (35.5)	85 (38.6)	0.066	0.554
Anatomical characteristics								
Dissection length	415.3±128.3	430.2±161.3	0.103	0.575	411.6±124.5	423.3±138.5	0.0891	0.732
Proximal thrombosis of false lumen			0.106	0.619			0.121	0.655
Patent	227 (45.0)	163 (40.0)			63 (40.1)	66 (44.3)		
Partial	163 (32.3)	137 (33.7)			54 (34.4)	44 (29.5)		
Complete	74 (14.7)	67 (16.5)			24 (15.3)	25 (16.8)		
ULP	41 (8.1)	40 (9.8)			16 (10.2)	14 (9.4)		
Malperfusion								
Superior mesenteric arteries	2 (0.4)	2 (0.5)	0.014	0.828	1 (0.5)	0 (0)	0.096	1.0
Renal arteries	20 (4.0)	14 (3.4)	0.028	0.68	9 (4.1)	9 (4.1)	<0.001	1.0
Common hepatic arteries	1 (0.2)	0 (0)	0.063	0.369	0	0	0	1
Lower-extremity arteries	7 (1.4)	6 (1.5)	0.007	0.911	3 (1.4)	1 (0.5)	0.096	0.616
Intraoperative details								
Timing of operation			0.257	<0.001			0.077	0.479
Acute	358 (70.9)	239 (58.7)			151 (68.6)	143 (65)		
Subacute	147 (29.1)	168 (41.3)			69 (31.4)	77 (35)		
Chimney technique	100 (19.8)	60 (14.7)	0.134	0.046	39 (17.7)	44 (20)	0.058	0.626
Adjunctive procedure	102 (20.2)	59 (14.5)	0.151	0.025	42 (19.1)	29 (13.2)	0.161	0.120
Hybrid approach	6 (1.2)	7 (1.7)	0.044	0.501	3 (1.4)	2 (0.9)	0.043	1.0

Values are expressed as number (percentage), mean±SD, or median (25th–75th percentile). Categorical variables are presented as number (percentage). BMI indicates body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; EOS, eosinophil count; PSM, propensity score matching; SBP, systolic blood pressure; SMD, standardized mean difference; ULP, ulcer-like projection; and WBC, white blood cell.

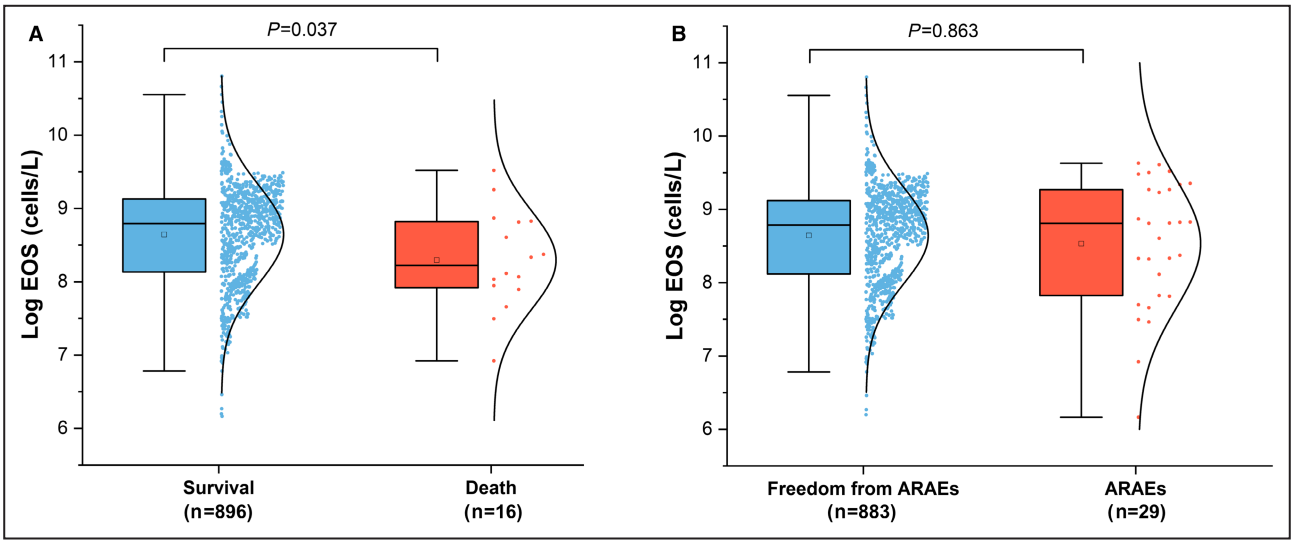

Figure 2. The different eosinophil count (EOS) levels in patients with different 30-day outcomes.
A, The EOS level in the death group was significantly lower than in the survival group. **B**, The EOS levels in the aortic-related adverse events (ARAEs) and freedom from ARAEs groups were not statistically different. The height of the boxes represents the general distribution of the data. The boxes contain a square in the middle (the mean value of the data) and a line (the median). Above and below the boxes are the error lines of the data. The right side of the box is the EOS value of each case, and the right-most curve represents the number of patients with different EOS values. The differences were assessed with Kruskal–Wallis test.

before and after matching. To visually analyze the functional interactions between continuous variables and outcomes, we utilized general additive models with restricted cubic splines to examine the nonlinear correlations between EOS and outcomes. Origin 8.0 (Origin Lab) software was used to create graphs. Statistical analyses were performed with R version 3.6.3 and EmpowerStats software (www.empowerstats.com). The statistical significance level was chosen at $P<0.05$.

RESULTS

Clinical Characteristics

Of the 912 patients included in the final analysis, the mean age was 58.5±13.1 years, 84.0% were men, 16 (1.8%) died, and 29 (3.2%) experienced ARAEs in the initial 30 days after TEVAR. Figure 2 depicts the difference in EOS levels among groups. Within 30 days after TEVAR, the EOS level in the death group was significantly lower (log [EOS]=8.29 vs 8.64/L, $P=0.037$) compared with the survival group. However, there was no statistical difference in EOS levels between the 30-day ARAEs and freedom from 30-day ARAEs groups (log [EOS]=8.53 vs 8.64/L, $P=0.863$).

To investigate the predictive efficacy of EOS on admission for 30-day all-cause mortality, a receiver operating characteristic curve analysis was performed. The best cutoff value was 7.4×10^6/L, which had an ideal sensitivity and specificity (area under the curve, 0.652 [95% CI, 0.518–0.786]) (Figure 3).

Patients were categorized depending on the EOS cutoff value, with EOS $<7.4\times10^6$/L (n=505) and EOS $\geq7.4\times10^6$/L (n=407). The baseline characteristics of the patients before and after PSM are shown in Table 1. In the unmatched population, the low EOS group had fewer men (81.6% vs 87.0%, $P=0.027$) and patients with smoking history (54.5% vs 68.3%, $P<0.001$). In addition, systolic blood pressure at admission and

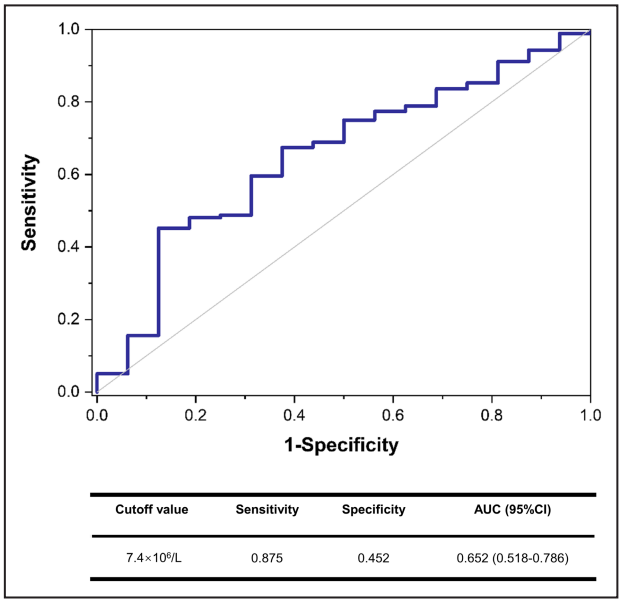

Figure 3. The receiver operating characteristic curves for eosinophil count counts in predicting 30-day all-cause death.
AUC indicates area under curve.

WBC count were significantly higher in the low EOS group (P=0.002 and P<0.001, respectively). Fewer patients were complicated with diabetes in the low EOS group (6.5% vs 11.3%, P=0.011). There were more patients with acute TBAD in the low EOS group (70.9% vs 58.7%, P<0.001). In addition, more patients received TEVAR with chimney and adjunctive approaches in the low EOS group (P=0.046 and P=0.025, respectively). After PSM, no statistically significant differences were found between the 2 groups for any of the baseline variables (P>0.05).

Short-Term Outcomes

The mean hospital stay after TEVAR was 12.4±6.8 in the low EOS group and 12.2±7.2 in the high EOS group. During hospitalization or 30 days after TEVAR, significantly higher mortality was observed in the low EOS group (4.1% vs 0%, P=0.007). However, there was no statistical difference in the adverse events after TEVAR (all P>0.05). The details of short-term outcomes are listed in Table 2.

There were 9 patients (4.1%) in the low EOS group who died within 30 days after TEVAR. One patient with a sudden stroke was referred to the emergency department 1 day after the TEVAR procedure. The conservative treatment did not work, and the patient died on the same day. Three patients died of sudden aortic rupture after the TEVAR procedure. Two patients underwent severe retrograde type A AD (RTAD) and died after the unsuccessful reintervention (4 days and 12 days after TEVAR). Two patients died 20 and 26 days after TEVAR from septic shock and respiratory failure caused by severe pneumonia. One patient died of acute organ failure at the intensive care unit 5 days after the surgery. In contrast, no patient died in the high EOS group within 30 days of TEVAR, and the difference was significantly different from the low EOS group (P=0.007).

The incidence of 30-day adverse events was 6.4% in the low EOS group and 3.6% in the high EOS group (P=0.189). A total of 3 aortic dilations were observed during the first 30 days, all in the high EOS group, with all of them receiving reintervention procedures and recovering. Four patients in the low EOS group experienced aortic rupture, with 2 patients surviving after reintervention. Five patients had type I/III endoleaks that were mild and left untreated with close follow-up. There were 2 patients with RTAD in the low EOS group, which was reported above. One patient with RTAD in the high EOS group fully recovered after immediate therapy. Four patients were found to have experienced strokes, with 3 in the low EOS group and 1 in the high EOS group. Two patients in the low EOS group had organ failures, one of whom survived after conservative treatment. No patient in the high EOS group was found to have organ failure.

Long-Term Outcomes

Table 3 shows the long-term results in the matched population, including 1-year all-cause mortality and ARAEs. The cumulative incidence rates for all-cause death, aortic-related death, ARAEs, and stroke are reported. A total of 20 deaths, including 15 aorta-related late deaths were found, 13 of which were caused by aortic rupture and RTAD. A total of 5 deaths were classified as nonaortic-related late deaths (heart failure, n=1; graft infection–related shock, n=1; and renal failure, n=2). The cause of the other death was unclear (n=1).

The cumulative incidence of 1-year all-cause death in the low EOS group was 7.95%, which in the high EOS group was 2.34%. Kaplan-Meier curve analysis showed that patients with an EOS <7.4×10^6/L had significantly worse survival than those with a higher EOS (P=0.008) (Figure 4A). The cumulative incidence of aortic-related death was also significantly higher in the low EOS group (5.98% vs 1.81%, P=0.023).

Table 2. Short-Term Outcomes in the Unmatched and Propensity Score–Matched Population

Variable	Unmatched groups			Propensity score–matched groups		
	Low EOS (n=505)	High EOS (n=407)	*P* value	Low EOS (n=220)	High EOS (n=220)	*P* value
Hospital stays of post-TEVAR, d	12.9±6.9	12.5±7.2	0.339	12.4±6.8	12.2±7.2	0.755
30-d mortality	14 (2.8)	2 (0.5)	0.009	9 (4.1)	0 (0)	0.007
Adverse events	27 (5.3)	12 (2.9)	0.075	14 (6.4)	8 (3.6)	0.189
Dilation	3 (0.6)	3 (0.7)	0.791	0 (0)	3 (1.4)	0.247
Malperfusion	1 (0.2)	2 (0.5)	0.442	0 (0)	1 (0.5)	0.799
Rupture	8 (1.6)	1 (0.3)	0.042	4 (1.8)	0 (0)	0.132
Type I/III endoleak	4 (0.8)	2 (0.5)	0.577	3 (1.4)	2 (0.9)	1.0
RTAD	3 (0.6)	2 (0.5)	0.835	2 (0.9)	1 (0.5)	0.693
Stroke	5 (1.0)	2 (0.5)	0.391	3 (1.4)	1 (0.5)	0.616
Organ failures	3 (0.6)	0 (0)	0.119	2 (0.9)	0 (0)	0.479

Values are expressed as mean±SD or number (percentage). EOS indicates eosinophil count; RTAD, retrograde type A aortic dissection; and TEVAR, thoracic endovascular aortic repair.

Table 3. Long-Term Outcomes in the Propensity Score–Matched Population

Variable	Low EOS (n=220)	High EOS (n=220)	*P* value
Cumulative incidence of 1-y all-cause death	7.95 (4.1–11.64)	2.34 (0.03–4.59)	0.008
Cumulative incidence of aortic-related death	5.98 (2.61–9.23)	1.81 (0–3.84)	0.023
Cumulative incidence of RTAD	2.28 (0.03–4.48)	2.59 (0.32–4.80)	0.697
Cumulative incidence of dilation	1.21 (0–2.85)	2.86 (0.35–5.31)	0.238
Cumulative incidence of malperfusion	2.70 (0.31–5.03)	0.55 (0–1.61)	0.108
Cumulative incidence of rupture	3.37 (0.88–5.80)	1.27 (0–3.02)	0.103
Cumulative incidence of type I/III endoleak	1.96 (0.04–3.85)	2.75 (0.33–5.11)	0.716
Cumulative incidence of stroke	3.79 (0.97–6.54)	2.80 (0.35–5.20)	0.584

Values are expressed as percentage (95% CI). Cumulative incidence estimates for 1-year all-cause death and aortic-related death, aortic-related adverse events, retrograde type A aortic dissection (RTAD), dilation, malperfusion, rupture, type I/III endoleak, and stroke with death as a competing risk. EOS indicates eosinophil count.

However, there was no statistical difference in the overall 1-year ARAEs between the 2 groups (11.25% vs 10.65%, *P*=0.759) (Figure 4B). The cumulative incidence of RTAD, dilation, malperfusion, rupture, type I/III endoleak, and stroke were not statistically significant between the 2 groups (all *P*>0.05). The Kaplan-Meier curves before PSM are shown in Figure S1.

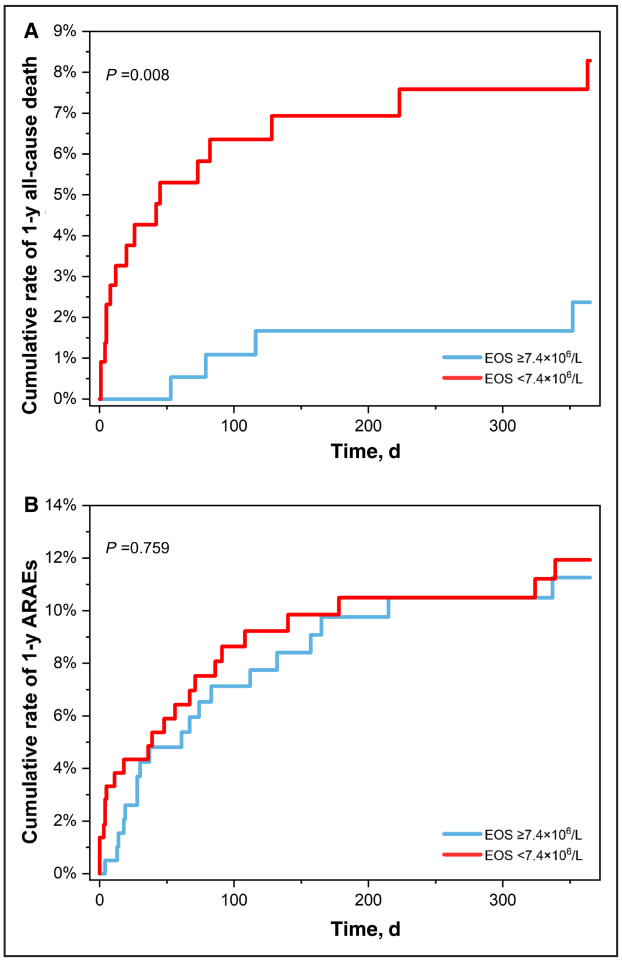

Figure 4. Kaplan-Meier survival analysis of 1-year outcomes after propensity score matching.
A, The cumulative incidence of 1-year all-cause mortality. **B**, The cumulative incidence of 1-year aortic-related adverse events (ARAEs). The differences were assessed with log-rank test. EOS indicates eosinophil count.

Table 4 reveals the findings of the Cox proportional hazard modeling evaluation. In the matched population, multivariable Cox regression analysis indicated that EOS (modeled as a continuous variable) was strongly linked with 1-year all-cause mortality (hazard ratio, 3.23 [95% CI, 1.20–8.33], *P*=0.019). Other independent predictors for long-term mortality included WBC count, platelet counts, hemoglobin, diabetes, stroke, chronic kidney disease, and pericardial effusion (Tables S1–S4). As a categorical variable, EOS <7.4×10^6/L was independently associated with a significantly increased risk of long-term mortality (hazard ratio, 4.00 [95% CI, 1.33–12.50], *P*=0.014). However, continuous EOS or EOS <7.4×10^6/L were not found to be related to 1-year ARAEs (*P*=0.676 and *P*=0.759, respectively).

The restricted cubic splines revealed nonlinear links between EOS and 1-year outcomes (Figure 5). Poor outcomes were strongly related to low EOS. Specifically, the EOS–mortality association was considerably negative, while the EOS–ARAE relationship was at first negative but later turned positive after a plateau. Notably, when EOS (x-axis) was 7.9×10^6/L, the log relative risk for 1-year mortality (y-axis) was approximately 0, demonstrating that EOS had no effect on the likelihood of death at this cutoff threshold (Figure 5A). In contrast, the log RR for 1-year ARAEs increased when EOS was <5.0×10^5/L and >2.0×10^7/L (Figure 5B).

DISCUSSION

The current study demonstrated that lower EOS was independently associated with increased risks of 30-day aortic rupture and 30-day and 1-year mortality.

EOS was formerly reported to be involved in allergy responses and host defense against parasites.[14] In recent studies, EOS has been found to be closely related to cardiovascular diseases.[15,16] Eosinophils were found

Table 4. Association of Preoperative EOS Counts on Long-Term All-Cause Death and ARAEs Before and After PSM

Variable	Unmatched groups				Propensity score–matched groups			
	Continuous EOS	*P* value	Low vs high	*P* value	Continuous EOS	*P* value	Low vs high	*P* value
1-y all-cause death								
Unadjusted HR (95% CI)	1.79 (1.09–2.94)	0.023	2.27 (1.12–4.76)	0.023	3.85 (1.41–10.00)	0.009	3.85 (1.32–11.11)	0.015
Adjusted HR (95% CI)	1.79 (1.00–3.44)	0.050	2.00 (0.89–4.35)	0.093	3.45 (1.28–9.09)	0.014	3.70 (1.22–11.11)	0.021
1-y ARAEs								
Unadjusted HR (95% CI)	1.01 (0.93–1.09)	0.839	1.16 (0.74–1.82)	0.518	1.04 (0.87–1.25)	0.676	1.10 (0.60–2.04)	0.759

Covariates for the multivariable model include age, sex, body mass index, smoking, systolic blood pressure, diastolic blood pressure, white blood cell counts, platelets, hemoglobin, creatinine, hypertension, diabetes, stroke, chronic obstructive pulmonary disease, chronic kidney disease, coronary artery disease, pericardial effusion, pleura effusion, timing of operation, chimney technique, adjunctive procedure, and hybrid approach. Variables with a *P* value <0.1 in univariable analysis were entered in the multivariable models (Details in Tables S1–S4). ARAEs indicates aortic-related adverse events; EOS, eosinophil count; HR, hazard ratio; and PSM, propensity score matching.

to be more abundant in patients with stroke compared with those with myocardial infarction thrombosis.[17] Sasmita et al[18] found that EOS increased dramatically in patients with cardiogenic shock accompanying acute myocardial infarction, and functioned as an independent predictive indicator for 30-day outcomes. Low eosinophil/monocyte ratio was linked with a higher risk of cardiovascular death or heart failure rehospitalization.[19] A retrospective study also revealed that eosinophil percentage impacted the prognosis of patients with acute type A AD.[10] To the best of our knowledge, this is the first research to explore the relationship between peripheral EOS and the short- and long-term outcomes of TEVAR-treated patients with TBAD.

Stress response may mediate the correlation between low EOS and poor outcomes of patients with TBAD. The "stress reaction" or "stress cascade" is a series of neuronal and endocrine changes that occur as a result of stressor-induced stimulation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system.[20] AD is often followed by acute pain, activation of the HPA and sympathetic nervous system axes, and a substantial quantity of released glucocorticoids.[20] The released glucocorticoids may limit eosinophil growth and promote its apoptosis, resulting in eosinophil reduction.[21] Eosinophils may therefore be one of the most essential stress markers. According to previous studies, female mice have a more

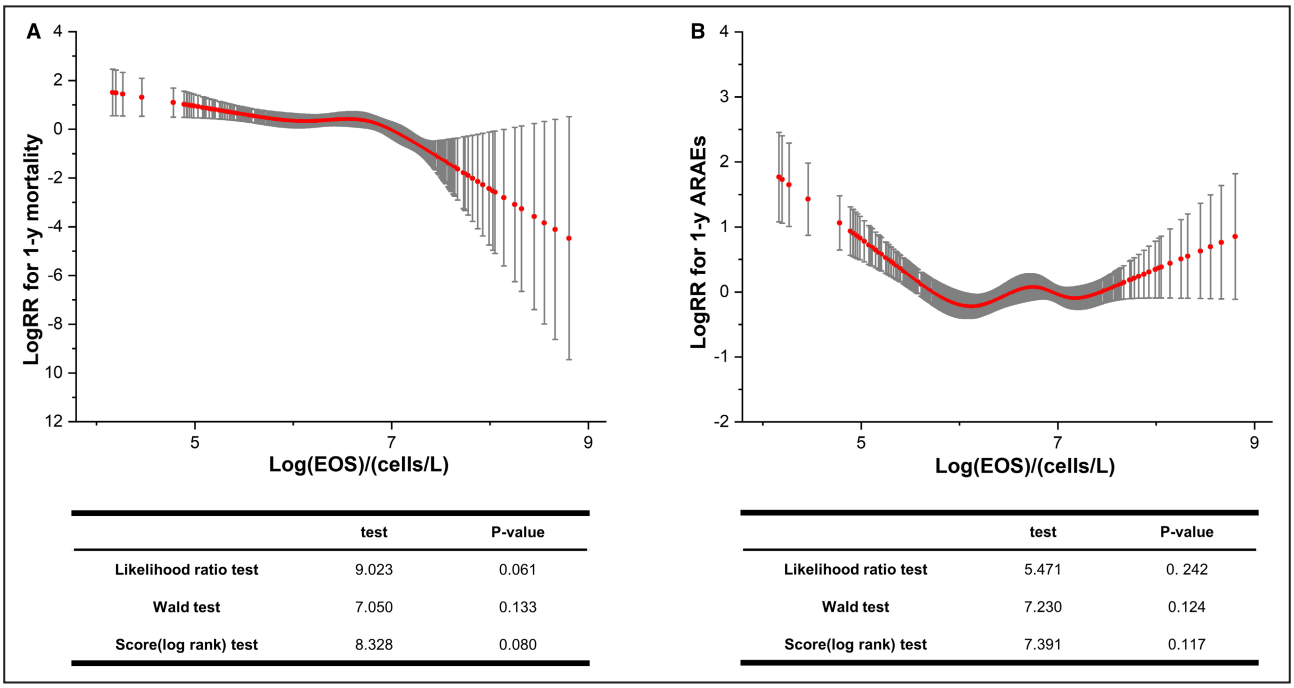

Figure 5. The association between eosinophil count (EOS) and the probability of 1-year mortality and aortic-related adverse events (ARAEs).
A, The relationship between EOS and log relative risk (RR) for 1-year mortality. **B**, The relationship between EOS and log RR for 1-year ARAEs. The red dots represent logRR of every logEOS value, while the gray bars are 95% confidence interval.

powerful HPA axis reaction than males, owing to crosstalk between the hypothalamic-pituitary-gonadal and HPA axes.[22] Women with TBAD have been proven by Takahashi et al[23] to have a higher proportion of intramural hematoma and higher in-hospital mortality than men. Our investigation found that women were notably more prevalent in the low EOS group, lending credence to that viewpoint. Besides, sympathetic nervous system activity is often associated with increased blood pressure, such as in the typical phenomenon "white-coat hypertension."[24] Another characteristic of the patients with low EOS in the current study was higher systolic blood pressure, demonstrating a higher physical stress reaction. Furthermore, the patients with acute TBAD had lower EOS than the patients with subacute TBAD (Table 1). Acute TEVAR has been associated with a higher risk of severe complications within a year.[25] The higher stress levels of patients with acute TBAD may be one of the underlying mechanisms of EOS leading to poor outcomes.

The low EOS group also had higher WBC and platelet levels. Despite the fact that the reduced EOS percentage was still a significant predictor of TBAD mortality even after adjusting for WBC and platelet levels, the inflammatory and thrombosis reaction may play a key role in the mechanism by which low EOS affects the prognosis of patients with TBAD. It has been shown that the release of a large number of cytokines, such as interleukin 5 may induce short-term chemotaxis of eosinophils to the interlayer site and reduce circulating eosinophils.[26] On the contrary, eosinophils are proinflammatory cells that secrete a vast variety of cytokines, growth factors, and chemokines to boost the inflammatory response in the aorta.[27,28]

In addition, eosinophils have been shown to be present in patients with in-stent thrombosis.[10] Eosinophils and platelets might interact at the false lumen, resulting in reciprocal activation. Platelets stimulate eosinophils as they travel to the thrombus, contributing to the formation of eosinophil extracellular traps, all of which contribute to thrombosis in the false lumen.[29] Eosinophils also produce tissue factors and phospholipid surfaces that activate the prothrombin complex to produce thrombin, further promoting fibrin formation.[30] Aorta segments with a partly thrombosed false lumen exhibited a considerably greater yearly aortic growth rate in individuals with acute TBAD.[31] This might explain why the rupture rate was higher in the low EOS group.

In comparison with others, EOS is a more comprehensive indicator. Eosinophils have been reported to be engaged in various inflammatory responses[32] and thrombosis pathology,[33] indicating their potential association with the occurrence and prognosis of patients with AD. Notably, EOS can be used to assess the intensity of stress reactivity and action of the HPA and sympathetic nervous system axes, which may not be replaced by other current markers. Representing a new mechanism, EOS may be incorporated into existing prognostic models of TBAD in further studies to improve their predictive performance and accuracy.

Compared with other detection methods, eosinophil testing is simple, rapid, and reproducible, making it an ideal clinical marker. In the current study, eosinophils were found for the first time to be potential prognostic indicators of patients with TBAD, which have high clinical value in perioperative risk stratification, postoperative monitoring, and prevention of complications.

Study Limitations

The present study has several limitations, including its retrospective design. In addition, clinical samples were not studied, and the role of eosinophils in the diagnosis of TBAD needs further study, including in combination with other biomarkers. Last, because of the relatively small sample size, the matched data may not exactly reflect the real situation.

CONCLUSIONS

The current study reveals that low EOS on admission was independently associated with higher short- and long-term mortality and aortic rupture for patients with TBAD undergoing TEVAR, implying its critical role in risk stratification. Special attention should be paid to patients with acute or subacute TBAD who have low EOS.

ARTICLE INFORMATION

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Affiliations

Department of Vascular Surgery, the First Affiliated Hospital of the Navy Medical University, Shanghai, China (K.Z., H.Z., J.M., Z. Zhao, L.Z., Z. Zeng, P.D., J.Z., Z.J.); Depaertment of General surgery, Jinling Hospital, Medical School of Nanjing University, Nanjing, China (Y.S.); and Department of Cardiology, Jinan Hospital of Integrated Traditional Chinese and Western Medicine, Jinan, Shandong, China (Q.Y.).

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Disclosures

None.

Supplemental Material

Tables S1–S4
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Univariate and multivariate Cox proportional hazard modeling analysis for 1-year all-cause mortality of unmatched population (continuous EOS).

	Univariate analysis			Multivariate analysis		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Age	1.02	(1.00, 1.05)	0.0608	1.01	(0.98, 1.04)	0.484
Male	1.29	(0.51, 3.31)	0.5896			
BMI	0.93	(0.84, 1.03)	0.1719			
Smoking	0.67	(0.36, 1.26)	0.2155			
SBP at admission (mmHg)	1	(0.99, 1.02)	0.6368			
DBP at admission (mmHg)	1	(0.97, 1.03)	0.8905			
EOS ($\times 10^6$/L)	1.79	(1.09, 2.94)	0.0232	1.79	(1.00, 3.44)	0.050
WBC ($\times 10^9$/L)	1.08	(1.01, 1.14)	0.0172	1.09	(1.02, 1.17)	0.012
Platelet ($\times 10^9$/L)	0.99	(0.99, 1.00)	0.0074	1	(0.99, 1.00)	0.109
Hemoglobin (g/L)	0.97	(0.96, 0.99)	0.0003	0.98	(0.97, 1.00)	0.047
Creatinine (μmol/L)	1	(1.00, 1.00)	0.0135	1	(1.00, 1.00)	0.157
Hypertension	2.15	(0.84, 5.49)	0.1109			
Diabetes	2.29	(1.01, 5.19)	0.0472	2.48	(1.02, 6.07)	0.046
Stroke	4.12	(1.90, 8.98)	0.0004	4.2	(1.80, 9.79)	0.001
COPD	0.66	(0.20, 2.14)	0.4889			
CKD	2.96	(1.24, 7.07)	0.0145	2.76	(1.15, 6.61)	0.023
CAD	2.01	(0.72, 5.67)	0.1851			
Pericardial effusion	2.51	(1.05, 6.00)	0.0377	1.91	(0.79, 4.63)	0.152
Pleural effusion	1.46	(0.78, 2.75)	0.2411			
Timing of operation						
Acute	1					
Sub-acute	0.99	(0.51, 1.90)	0.9748			
Chimney technique	1.21	(0.56, 2.63)	0.632			
Adjunctive procedure	1.2	(0.55, 2.61)	0.6454			
Hybrid approach	1.91	(0.26, 13.92)	0.5228			

EOS, eosinophil count; HR = hazard ratio; CI = confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CAD, coronary artery disease.

Table S2. Univariate and multivariate Cox proportional hazard modeling analysis for 1-year all-cause mortality of unmatched population (Low vs. High EOS).

	Univariate analysis			Multivariate analysis		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Age	1.02	(1.00, 1.05)	0.061	1.01	(0.98, 1.04)	0.437
Male	1.29	(0.51, 3.31)	0.590			
BMI	0.93	(0.84, 1.03)	0.172			
Smoking	0.67	(0.36, 1.26)	0.216			
SBP at admission (mmHg)	1	(0.99, 1.02)	0.637			
DBP at admission (mmHg)	1	(0.97, 1.03)	0.891			
EOS <7.4× 10^6/L)	2.27	(1.12, 4.76)	0.023	2.00	(0.89, 4.35)	0.093
WBC (× 10^9/L)	1.08	(1.01, 1.14)	0.017	1.09	(1.02, 1.17)	0.008
Platelet (× 10^9/L)	0.99	(0.99, 1.00)	0.0074	1.00	(0.99,1.00)	0.080
Hemoglobin (g/L)	0.97	(0.96, 0.99)	<0.001	0.98	(0.99, 1.00)	0.039
Creatinine (μmol/L)	1	(1.00, 1.00)	0.014	1.00	(1.00, 1.00)	0.208
Hypertension	2.15	(0.84, 5.49)	0.111			
Diabetes	2.29	(1.01, 5.19)	0.047	2.34	(0.95, 5.74)	0.064
Stroke	4.12	(1.90, 8.98)	<0.001	4.06	(1.74, 9.49)	0.001
COPD	0.66	(0.20, 2.14)	0.489			
CKD	2.96	(1.24, 7.07)	0.015	2.88	(1.21, 6.89)	0.017
CAD	2.01	(0.72, 5.67)	0.185			
Pericardial effusion	2.51	(1.05, 6.00)	0.038	1.87	(0.77, 4.56)	0.167
Pleural effusion	1.46	(0.78, 2.75)	0.241			
Timing of operation						
Acute	1					
Sub-acute	0.99	(0.51, 1.90)	0.975			
Chimney technique	1.21	(0.56, 2.63)	0.632			
Adjunctive procedure	1.2	(0.55, 2.61)	0.645			
Hybrid approach	1.91	(0.26, 13.92)	0.523			

EOS, eosinophil count; HR = hazard ratio; CI = confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CAD, coronary artery disease.

Table S3. Multivariate Cox proportional hazard modeling analysis for 1-year all-cause mortality of propensity score-matched population (continuous EOS).

	Multivariate analysis		
	HR	**95% CI**	**P-value**
EOS ($\times 10^6$/L)	3.45	(1.28, 9.09)	0.014
Platelet ($\times 10^9$/L)	0.99	(0.99, 1.01)	0.458
Adjunctive procedure	0.88	(0.26, 3.01)	0.837

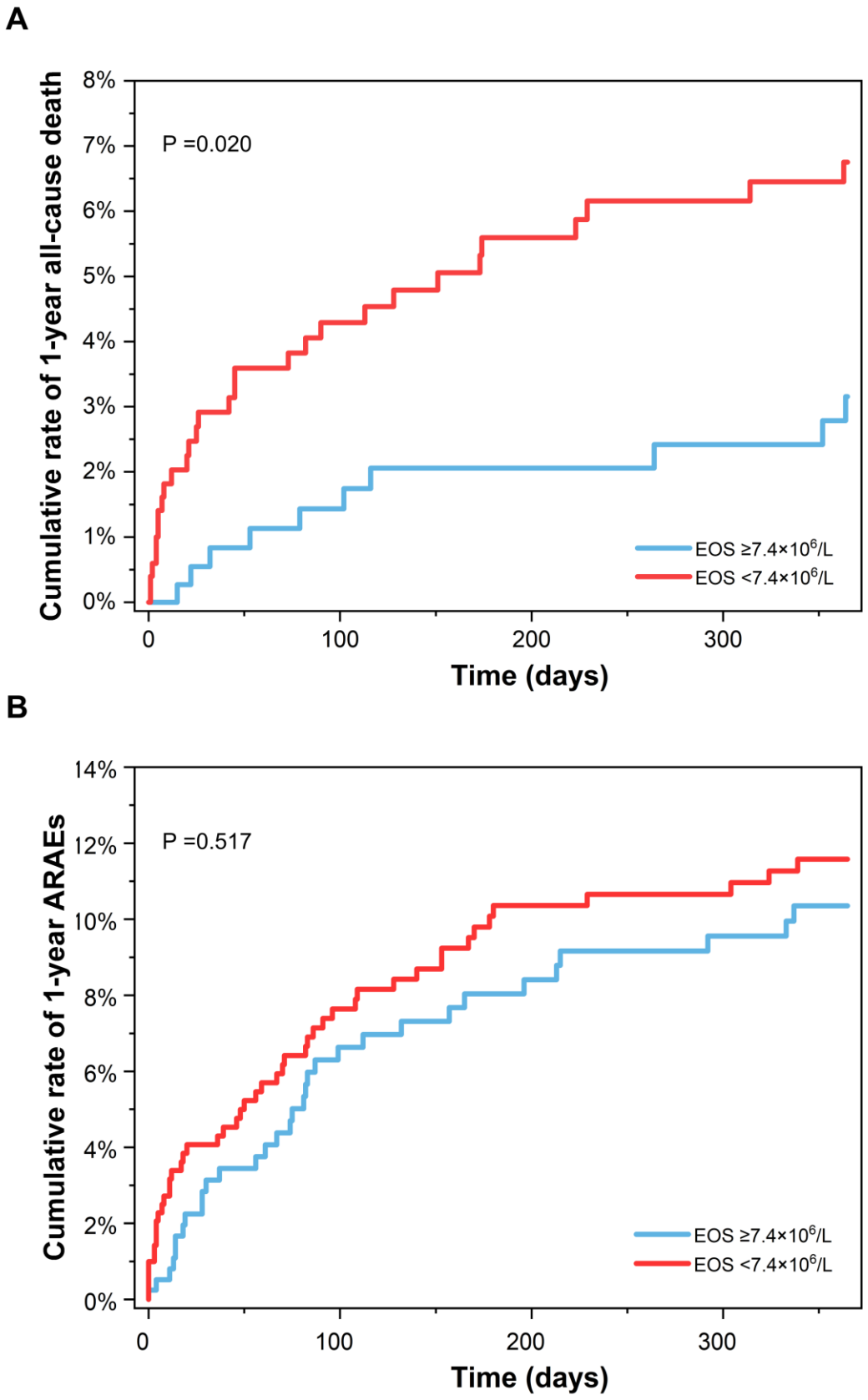
EOS, eosinophil count.

Table S4. Multivariate Cox proportional hazard modeling analysis for 1-year all-cause mortality of propensity score-matched population (Low vs. High EOS).

	Multivariate analysis		
	HR	**95% CI**	**P-value**
EOS <7.4× 10^6/L)	3.70	(1.22, 11.11)	0.021
Platelet (× 10^9/L)	0.99	(0.99, 1.00)	0.072
Adjunctive procedure	0.83	(0.24, 2.85)	0.771

EOS, eosinophil count.

Figure S1. Kaplan-Meier survival analysis of 1-year outcomes before propensity score matching.



A. The cumulative incidence of 1-year all-cause mortality. B. The cumulative incidence of 1-year ARAE. The differences were assessed with log-rank test. EOS, eosinophil count; ARAEs, aortic-related adverse events.