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Impact of the De Ritis Ratio on the Prognosis of Patients with Stable Coronary Artery Disease Undergoing Percutaneous Coronary Intervention

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to emphasize the impact of the aspartate aminotransferase-to-alanine aminotransferase ratio (De Ritis ratio) on the prognosis of patients with stable coronary artery disease (SCAD) undergoing percutaneous coronary intervention (PCI).

Material/Methods: Patients with SCAD who underwent elective PCI at Shinonoi General Hospital were included. SCAD was defined as epicardial coronary artery diameter stenosis ≥90% or epicardial coronary artery diameter stenosis ≥75% accompanied by symptoms or stress-induced myocardial ischemia. Clinical data were collected, and cardiovascular events were followed after discharge. One-way Cox proportional risk analysis was performed to assess the risk stratification value of the De Ritis ratio, using major adverse cardiac and cerebrovascular events (MACCE) and all-cause mortality as the primary and secondary endpoints, respectively. The independent risk stratification value was evaluated by multivariate Cox proportional risk analysis.

Results: Among 204 patients with SCAD undergoing PCI, during a median follow-up period of 706 days (24 months), 13.7% (28/204) patients experienced MACCE, and 8.8% (18/204) experienced all-cause mortality. Multifactorial Cox regression analysis revealed that a high De Ritis ratio was an independent risk factor for MACCE (HR=2.96, 95% CI: 1.29-6.78, *P*=0.01) and all-cause mortality (HR=3.61, 95% Cl: 1.31-9.86, *P*=0.012). The sensitivity analysis further confirmed the incremental value of the De Ritis ratio for adverse cardiovascular events.

Conclusions: A high De Ritis ratio was an independent and valuable risk stratification factor for MACCE and all-cause mortality in patients with SCAD after PCI.

Keywords: Alanine Transaminase • Aspartate Aminotransferases • Coronary Artery Disease • Prognosis

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Background

Percutaneous coronary intervention (PCI) has reduced the incidence of major adverse cardiovascular and cerebrovascular events (MACCE) in patients with stable coronary artery disease (SCAD) with sufficient evidence of ischemia; however, some patients still have a poor prognosis [1]. Recent studies have shown that a high aspartate aminotransferase-to-alanine aminotransferase ratio (De Ritis ratio) is associated with a worse prognosis in patients with acute myocardial infarction [2,3] and acute heart failure [4]. Study also have shown that an elevated De Ritis ratio on admission was significantly associated with intensive care unit mortality and hospital mortality after cardiac arrest [5]. The De Ritis ratio reflects the severity of hepatic insufficiency [6], and patients with coronary artery disease complicated by hepatic insufficiency have a high incidence of perioperative complications [7,8]. However, research on the relationship between the De Ritis ratio and the prognosis of patients with SCAD undergoing PCI is still lacking. This study aimed to evaluate the relationship between the De Ritis ratio and prognosis in patients undergoing elective PCI for SCAD.

Material and Methods

Study Population

The population in this study was obtained from a single-center retrospective cohort using open data [9]. The study included patients with SCAD who underwent elective PCI at Shinonoi General Hospital from October 2014 to October 2017. SCAD was defined as epicardial coronary artery diameter stenosis ≥90% or epicardial coronary artery diameter stenosis ≥75% accompanied by exercise-induced chest pain or stress-induced myocardial ischemia, confirmed by any clinical stress test. Patients with diagnoses of old myocardial infarction and malignant tumors were excluded. Finally, 204 patients were included in this study. The study was approved by the Ethics Committee of Shinonoi General Hospital, and written informed consent was obtained from all patients. Our study was a secondary analysis based on the data described above, and all patient information was kept anonymous. Therefore, informed patient consent and ethics committee approval were not required.

Data Collation and Variable Definition

Clinical features, including clinical characteristics, medical history, major risk factors for coronary artery disease, complications, laboratory tests, electrocardiogram, echocardiography, angiography data, and discharge medications, were collected. A multivessel lesion was defined as a 3-vessel lesion. The patients were subsequently followed up after discharge to document all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke outcomes. The main endpoint of this study was MACCE, including all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke. The secondary endpoint was all-cause mortality.

Statistical Analysis

Continuous variables are expressed as mean and standard deviation, and the *t* test was used for comparison between the groups. Categorical variables are expressed as absolute values and proportions, and the chi-square test was used for comparison between the groups. In this study, it was assumed that the missing clinical features occurred randomly, and multiple interpolations were performed using the random forest method in the multivariate imputation by chained equation (MICE) function of the MICE package, assuming missing clinical features. The integrated dataset was randomly split using the CreateDataPartition function of the caret package. According to the De Ritis ratio, patients were divided into low (<1.85) and high (≥1.85) De Ritis ratio groups. Kaplan-Meier survival charts were plotted and compared using the log-rank test. One-way Cox proportional risk analysis was conducted with primary and secondary endpoints as predicted outcomes. Multivariate calibration was conducted using age, body mass index (BMI), serum albumin, C-reactive protein, and multivessel lesion as covariates to assess the independent risk stratification value of the De Ritis ratio. Furthermore, in the sensitivity analysis, Cox proportional risk model A was fitted with age, BMI, serum albumin, C-reactive protein, and multivessel lesion as dependent variables. Model B was fitted by incorporating the De Ritis ratio into model A. The comparison between models A and B was used to evaluate the incremental predictive value of the De Ritis ratio. A *P* value <0.05 was considered as statistically significant. All statistical analyses were performed using R 4.1.3 software (The R foundation for Statistical Computing, Vienna, Austria).

Results

Population Information

A total of 204 patients who underwent PCI for SCAD were included in the study (**Table 1**). Among these patients (142 men, 69.6%), 74.0% had hypertension and 35.8% had diabetes mellitus. The high De Ritis ratio group had a higher age and lower BMI, albumin levels, hemoglobin concentration, and creatinine clearance than the low De Ritis ratio group. During the median follow-up period of 706 days (24 months), MACCE occurred in 13.7% (28/204) of patients, and all-cause mortality occurred in 8.8% (18/204). MACCE and all-cause mortality occurred in 33.3% and 10.7% of the patients in the high De Ritis ratio group, respectively, compared with 10.7% and 6.2% in the low De Ritis ratio group.

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Table 1. Clinical data of the study population.

	Overall population		Low De Ritis ratio (n=177)		High De Ritis ratio (n=27)		p value
Age (years), n (%)							<0.001
<60	22	(10.8)	21	(11.9)	1	(3.7)	
60-69	58	(28.4)	56	(31.6)	2	(7.4)	
70-79	71	(34.8)	61	(34.5)	10	(37.0)	
≥80	53	(26.0)	39	(22.0)	14	(51.9)	
Men, n (%)	142	(69.6)	127	(71.8)	15	(55.6)	0.139
BMI (kg/m^2), n (%)							0.002
<18.5	17	(8.3)	13	(7.3)	4	(14.8)	
18.5-24.9	119	(58.3)	98	(55.4)	21	(77.8)	
≥25.0	68	(33.3)	66	(37.3)	2	(7.4)	
Alb (g/dL) ≥4.0, n (%)	115	(56.4)	106	(59.9)	9	(33.3)	0.017
Hb (g/dL) (mean (SD))	13.58	(2.01)	13.80	(1.92)	12.14	(2.02)	<0.001
eGFR(mL/min/1.73 m^2) (mean [SD])	61.32	(24.61)	64.09	(23.42)	43.15	(24.92)	<0.001
CRP (mg/dL), n (%)							0.964
0.01-0.03	34	(16.7)	30	(16.9)	4	(14.8)	
0.04-0.11	64	(31.4)	55	(31.1)	9	(33.3)	
0.12-0.33	55	(27.0)	47	(26.6)	8	(29.6)	
0.34-9.20	51	(25.0)	45	(25.4)	6	(22.2)	
AST (mean (SD))	24.66	(10.93)	24.58	(11.02)	25.22	(10.52)	0.776
ALT (mean (SD))	20.90	(12.19)	22.42	(12.24)	10.93	(5.17)	<0.001
LVEF (mean (SD))	63.36	(9.88)	63.51	(9.59)	62.33	(11.81)	0.564
OCI, n (%)	35	(17.2)	28	(15.8)	7	(25.9)	0.306
PAD, n (%)	53	(26.0)	45	(25.4)	8	(29.6)	0.819
Hypertension, n (%)	151	(74.0)	132	(74.6)	19	(70.4)	0.819
Diabetes mellitus, n (%)	73	(35.8)	65	(36.7)	8	(29.6)	0.617
Smoker, n (%)	101	(49.5)	94	(53.1)	7	(25.9)	0.015
Aspirin, n (%)	202	(99.0)	176	(99.4)	26	(96.3)	0.622
Thienopiridines, n (%)	200	(98.0)	174	(98.3)	26	(96.3)	1.000
Warfarin, n (%)	5	(2.5)	3	(1.7)	2	(7.4)	0.263
DOAC, n (%)	21	(10.3)	18	(10.2)	3	(11.1)	1.000
Statins, n (%)	111	(54.4)	101	(57.1)	10	(37.0)	0.082
ACEI/ARB, n (%)	106	(52.0)	90	(50.8)	16	(59.3)	0.543
βblocker, n (%)	55	(27.0)	46	(26.0)	9	(33.3)	0.57
MRA, n (%)	11	(5.4)	10	(5.6)	1	(3.7)	1.000

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Table 1 continued. Clinical data of the study population.

	Overall population	Low De Ritis ratio (n=177)	High De Ritis ratio (n=27)	p value
Bifurcation lesions, n (%)	101 (49.5)	85 (48.0)	16 (59.3)	0.378
Multivessel lesions, n (%)	53 (26.0)	47 (26.6)	6 (22.2)	0.808
LMT, n (%)	13 (6.4)	12 (6.8)	1 (3.7)	0.852
Calcification lesions, n (%)	29 (14.2)	23 (13.0)	6 (22.2)	0.326
CTO, n (%)	12 (5.9)	12 (6.8)	0 (0.0)	0.339

BMI – body mass index; Alb – serum albumin; Hb – hemoglobin; eGFR – estimated glomerular filtration rate; CRP – C-reactive protein; LVEF – left ventricular ejection fraction; OCI – old cerebral infarction; PAD – peripheral artery disease; DOAC – direct oral anticoagulant; MRA – mineralocorticoid receptor antagonists; LMT – left main trunk; CTO – chronic total occlusion.

Single Factor Analysis

Taking MACCE and all-cause mortality as dependent variables and the De Ritis ratio as the independent variable, the results of the univariate analysis showed that a high De Ritis ratio was related to MACCE (hazard ratio [HR]=3.60, 95% CI: 1.60-7.90, *P*=0.002) and all-cause mortality (HR=4.70, 95% CI: 1.80-12.00, *P*=0.001). The Kaplan-Meier analysis showed the same results (**Figure 1**).

Multivariate Regression Analysis

In the multivariate Cox regression analysis, MACCE and all-cause mortality were used as dependent variables, De Ritis ratio as the independent variable, and age, BMI, serum albumin, and C-reactive protein as covariates. Similar to the single-factor analysis, the De Ritis ratio was related to MACCE (HR=2.96, 95% CI: 1.29-6.78, *P*=0.01) and all-cause mortality (HR=3.61, 95% CI: 1.31-9.86, *P*=0.012) (**Figure 2**).

Sensitivity Analysis

Cox proportional risk model A was fitted with age, BMI, serum albumin, and C-reactive protein, and model B was fitted by incorporating the De Ritis ratio into model A. The De Ritis ratio increased the predictive value of model B compared with that of model A for MACCE and all-cause mortality, with the improved concordance index during the follow-up period (**Figure 3**).

Discussion

This study evaluated the correlation between the De Ritis ratio and prognosis in patients with SCAD undergoing selective PCI. The results revealed that a high De Ritis ratio was independently and significantly associated with a high risk of MACCE and all-cause mortality, and that the De Ritis ratio was another valuable risk stratification factor.

Previous studies have demonstrated that a low BMI [10], low serum albumin [9], high C-reactive protein level [11], and multivessel lesion [12] are associated with a high risk of MACCE in patients with SCAD. Also, Alqahtani et al found an increased risk of acute myocardial infarction and in-hospital mortality in patients undergoing PCI for liver cirrhosis compared with in those with non-liver cirrhosis [13]. Thus, Steininger et al included 1355 patients with acute myocardial infarction and attempted to investigate the predictive potential of the De Ritis ratio on the prognosis of patients after acute myocardial infarction from a long-term perspective. Those results showed that the De Ritis ratio was a strong and independent predictor of their long-term mortality, with an adjusted HR of 1.23 (95% CI: 1.07-1.42, *P*=0.004) [3]. Additionally, Maeda et al discussed the relationship between the De Ritis ratio and prognosis of patients with acute heart failure and found that a high De-Ritis ratio was an independent prognostic factor for acute heart failure [4]. A retrospective cohort study including 6264 patients undergoing cardiovascular surgery also showed that a high De Ritis ratio was positively correlated with mortality [14]. More importantly, consistent with the above studies, the De Ritis ratio was associated with the risk of MACCE and all-cause mortality after adjustment for previous risk factors with long-term follow-up, and the introduction of the De Ritis ratio in the previous risk factors resulted in improved risk prediction performance in patients with SCAD undergoing selective PCI.

Previous studies have shown that the degree of hepatic fibrosis is related to the development of atherosclerosis [15]. Chronic liver disease and coronary artery disease have similar pathogeneses, but the exact mechanism remains unclear. Some possible pathways include insulin resistance, lipid disorders, inflammation [16], and increased production of various thromboplastins by the liver, such as fetuin A, which promotes the formation of atherosclerotic plaques and accelerates vascular calcium deposition in patients with hepatic fibrosis [17]. Gjin et al showed that alanine aminotransferase was negatively

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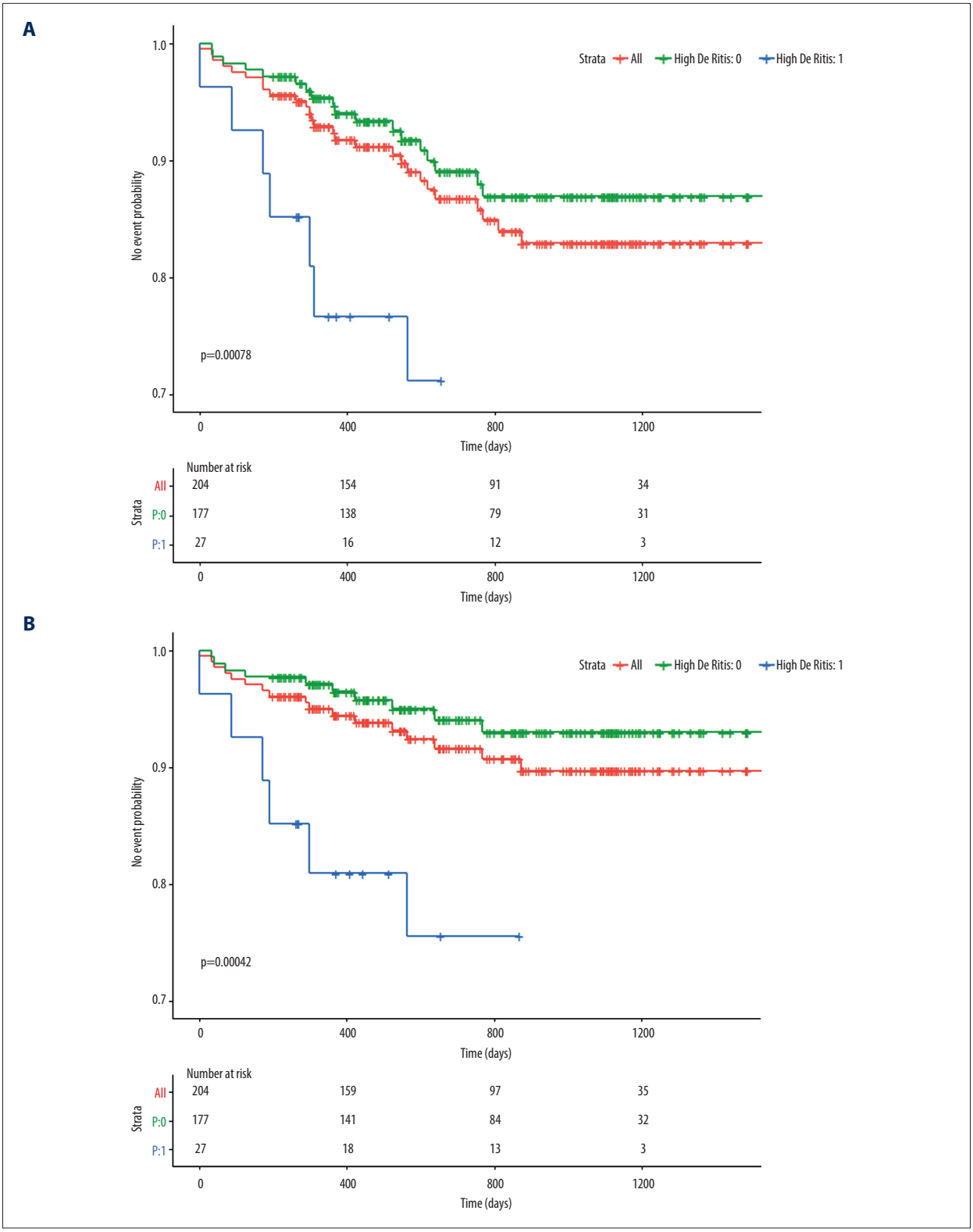

Figure 1. Kaplan-Meier survival curves of (**A**) major adverse cardiac and cerebrovascular events and (**B**) all-cause mortality in patients with a high De Ritis ratio and a low De Ritis ratio in 2 years after percutaneous coronary intervention. Created with R software (version 4.1.3; The R foundation for Statistical Computing, Vienna, Austria). 0 – low De Ritis ratio; 1 – high De Ritis ratio.

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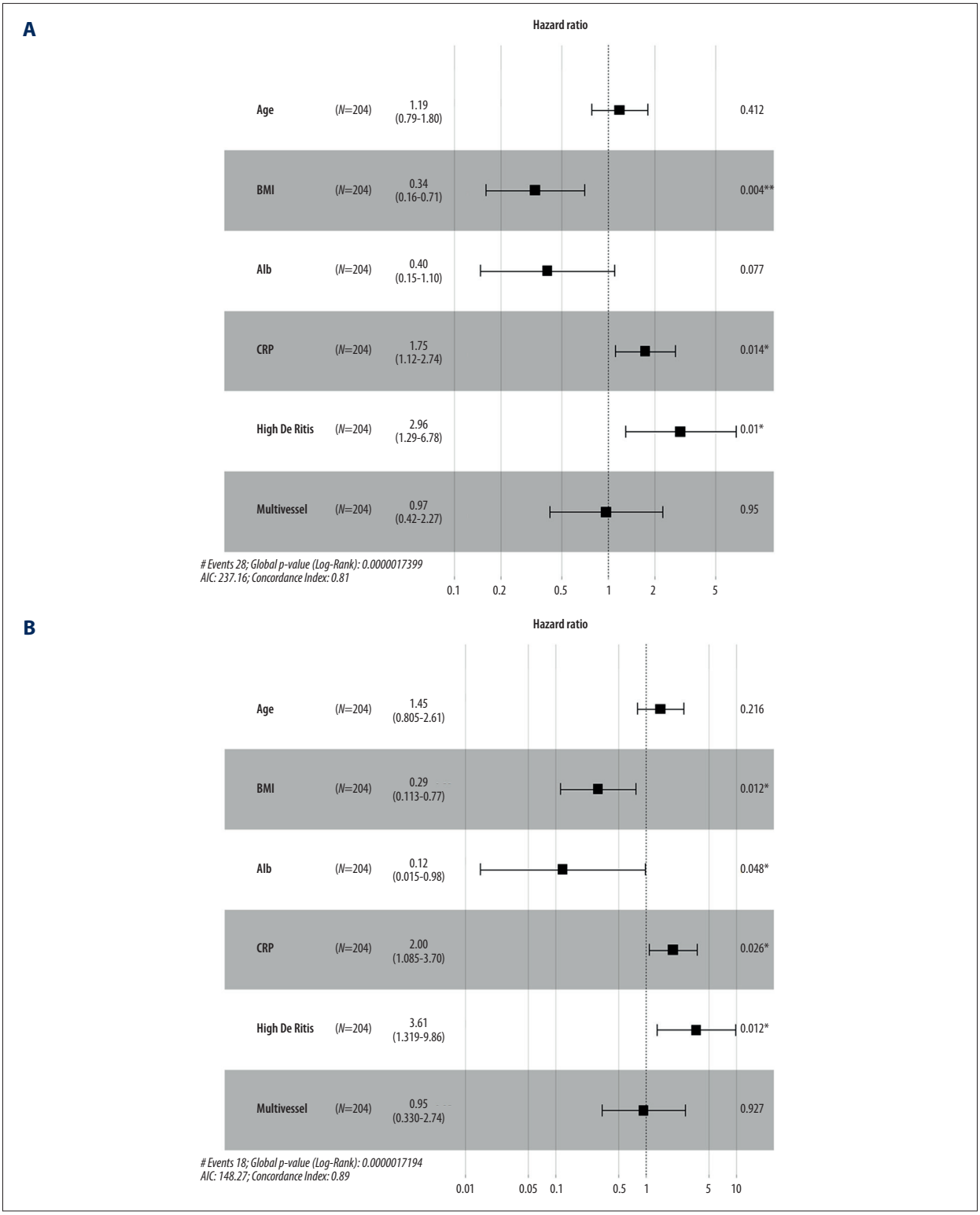

Figure 2. Forest plot of Cox regression analysis of (**A**) major adverse cardiac and cerebrovascular events and (**B**) all-cause mortality in 2 years after percutaneous coronary intervention. Created with R software (version 4.1.3; The R foundation for Statistical Computing, Vienna, Austria). Age – age (years), divided into 4 levels: <60, 60-69, 70-79, and ≥80; BMI – body mass index (kg/m^2), divided into 3 levels: <18.5, 18.5-24.9, and ≥25.0 [10]; Alb – serum albumin (g/dL), divided into 2 levels <4.0 and ≥4.0 [9]; CRP – C-reactive protein (mg/dL), divided into 4 levels: 0.01-0.03, 0.04-0.11, 0.12-0.33, and 0.34-9.20 [11].

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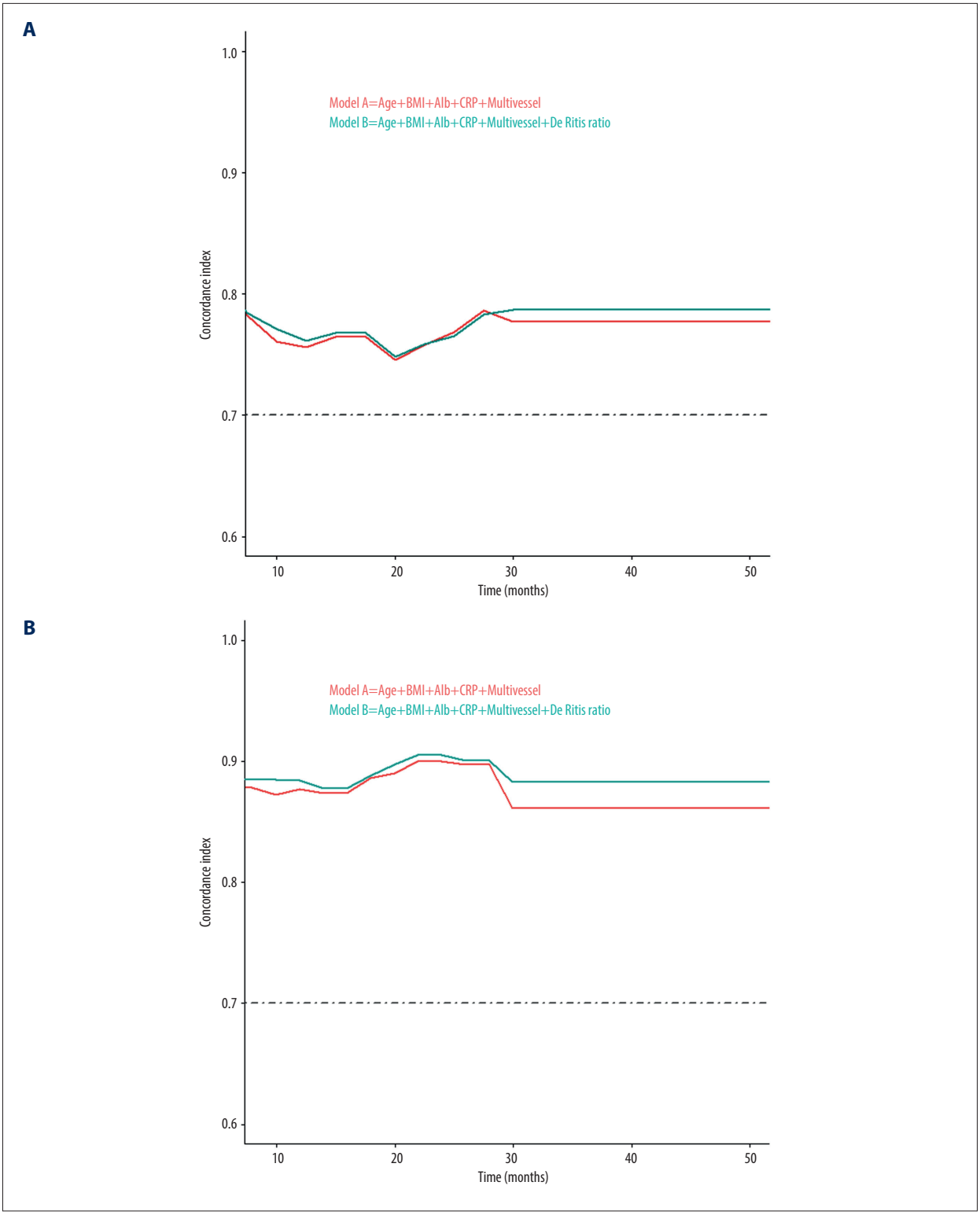

Figure 3. Concordance index of (**A**) major adverse cardiac and cerebrovascular events and (**B**) all-cause mortality predicted by model A and model B during the follow-up period. Created with R software (version 4.1.3; The R foundation for Statistical Computing, Vienna, Austria). Model A was fitted with age, BMI, albumin, C-reactive protein levels, and multivessel which have been proven to have prognostic value. Model B was a new model that introduced the De Ritis ratio to model A. BMI – body mass index; CRP – C-reactive protein; Alb – serum albumin; Multivessel – multivessel lesion.

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correlated with 3-year cardiovascular mortality in patients with coronary artery disease diagnosed as having no abnormal liver function and that low alanine aminotransferase levels may reflect the risk of cardiovascular disease better than traditional risk factors [18]. Furthermore, identifying the cause of liver damage and active intervention can help to optimize secondary prevention strategies and improve patient prognosis.

This study has several limitations. First, this was a post hoc analysis of a retrospective cohort study, which inevitably had selection or regression bias. Second, the population analyzed in the study was solely from a Japanese hospital, and the research conclusion needs more analysis of populations from different regions and races. Third, patients with high levels of both aspartate aminotransferase and alanine aminotransferase can have evident liver damage, but the De Ritis ratio may not be high, which is the limitation of this ratio.

Conclusions

This study demonstrated that a high De Ritis ratio in patients with SCAD undergoing PCI was an independent and valuable risk stratification factor for MACCE and all-cause mortality. This conclusion needs to be confirmed in a multi-center study.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Wang Y, Wang W, Jia S, et al. Development of a nomogram for the prediction of in-hospital mortality in patients with acute St-elevation myocardial infarction after primary percutaneous coronary intervention: A multicentre, retrospective, observational study in Hebei Province, China. BMJ Open. 2022;12(2):e056101
2. Ndrepepa G, Holdenrieder S, Kastrati A. Prognostic value of De Ritis ratio in patients with acute myocardial infarction. Clin Chim Acta. 2022;535:75-81
3. Steininger M, Winter M P, Reiberger T, et al. De-Ritis ratio improves long-term risk prediction after acute myocardial infarction. J Clin Med. 2018;7(12):474
4. Maeda D, Sakane K, Kanzaki Y, et al. Relation of aspartate aminotransferase to alanine aminotransferase ratio to nutritional status and prognosis in patients with acute heart failure. Am J Cardiol. 2021;139:64-70
5. Lu Z, Ma G, Chen L. De-Ritis ratio is associated with mortality after cardiac arrest. Dis Markers. 2020;2020:8826318
6. Giannini E, Botta F, Fasoli A, et al. Progressive liver functional impairment is associated with an increase in Ast/Alt ratio. Dig Dis Sci. 1999;44(6):1249-53
7. Wu VC, Chen SW, Chou AH, et al. Nationwide cohort study of outcomes of acute myocardial infarction in patients with liver cirrhosis: A nationwide cohort study. Medicine (Baltimore). 2020;99(12):e19575
8. Hillerson D, Ogunbayo G O, Salih M, et al. Outcomes and characteristics of myocardial infarction in patients with cirrhosis. J Invasive Cardiol. 2019;31(7):E162-69
9. Suzuki S, Hashizume N, Kanzaki Y, et al. Prognostic significance of serum albumin in patients with stable coronary artery disease treated by percutaneous coronary intervention. PLoS One. 2019;14(7):e0219044
10. Liu X, Liu P. Body mass index and major adverse cardiovascular events: A secondary analysis based on a retrospective cohort study. Med Sci Monit. 2020;26:e919700
11. Luo F, Feng C, Zhuo C. C-reactive protein and all-cause mortality in patients with stable coronary artery disease: A secondary analysis based on a retrospective cohort study. Med Sci Monit. 2019;25:9820-28
12. Bauters C, Deneve M, Tricot O, et al. Prognosis of patients with stable coronary artery disease (from the coronor study). Am J Cardiol. 2014;113(7):1142-45
13. Alqahtani F, Balla S, Alhajji M, et al. Temporal trends in the utilization and outcomes of percutaneous coronary interventions in patients with liver cirrhosis. Catheter Cardiovasc Interv. 2020;96(4):802-10
14. Nam JS, Kim WJ, An SM, et al. Age-dependent relationship between preoperative serum aminotransferase and mortality after cardiovascular surgery. Aging (Albany NY). 2019;11(20):9060-74
15. Turan Y. The nonalcoholic fatty liver disease fibrosis score is related to epicardial fat thickness and complexity of coronary artery disease. Angiology. 2020;71(1):77-82
16. Lonardo A, Nascimbeni F, Mantovani A, et al. Hypertension, diabetes, atherosclerosis and nash: Cause or consequence? J Hepatol. 2018;68(2):335-52
17. Sato M, Kamada Y, Takeda Y, et al. Fetuin – a negatively correlates with liver and vascular fibrosis in nonalcoholic fatty liver disease subjects. Liver Int. 2015;35(3):925-35
18. Ndrepepa G, Holdenrieder S, Colleran R, et al. Inverse association of alanine aminotransferase within normal range with prognosis in patients with coronary artery disease. Clin Chim Acta. 2019;496:55-61

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