Predictive Factors of Medium-Large Coronary Artery Aneurysm in Children with Acute Kawasaki Disease: A Retrospective Cohort Study

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Abstract

Background: The severity of the cardiac complications resulting from Kawasaki disease (KD) appears to be directly correlated to the magnitude of the coronary artery aneurysm (CAA). However, there remains some unclear about the risk factors for medium-large CAA identified after acute KD.

Methods: We analyzed 90 patients diagnosed with CAA in KD hospitalized from January 2013 through August 2021. Patients were stratified based on the coronary artery z-score adjusted for body surface area as the medium-large CAA group and small-sized CAA group. The association of baseline characteristics was investigated within the groups. Multivariable logistic regression analyses were performed to evaluate potential risk factors associated with medium-large CAA development.

Results: In total, 353 pediatric cases with KD were investigated during the study period, of whom 90 (25.5%) presented with CAA, including medium-large CAA in 20 patients (5.7%) after acute KD. The medium-large CAA group showed significantly higher Harada risk scores, the incidence of thrombosis, serum globulin concentration values, proportions of C-reactive protein > 40 mg/L, proportions of albumin < 35 g/L, and lower values of albumin-to-globulin ratio (A/G ratio) than those in the small-sized CAA group ($P < 0.05$). Medium-large CAA was significantly associated with the A/G ratio (odds ratio, 3.503; 95% confidence interval [CI]: 1.068–11.492). The area under the receiver operating characteristic curve was 0.684 (95% CI: 0.558–0.810), and the cutoff point of 1.35 showed a sensitivity and specificity for predicting medium-large CAA of 80% and 59%, respectively.

Conclusions: A lower A/G ratio independently predicts medium-large CAA in patients with KD. Medium-large CAA is associated with greater odds of developing thrombosis. Thus, close monitoring with routine echocardiography is recommended.

Introduction

Coronary artery aneurysm (CAA) is a potentially fatal cardiac complication resulting from Kawasaki disease (KD) and has gradually become the leading cause of acquired heart disease in children over recent years [1–3]. Globally, China is among the countries with a high prevalence of KD. Epidemiological investigations revealed that the incidence of coronary artery lesions (CAL) during the acute phase decreased from 19.8% in 1998 to 9.1% in 2017 in Shanghai, one of the areas in China with the highest incidence of KD, despite the timely administration of large doses of intravenous immunoglobulin (IVIG) and aspirin therapy. The incidence of medium-large coronary aneurysms was as high as 3.4% [4]. If the coronary artery diameter in the acute phase exceeds 6 mm, the appearance of stenotic lesions increases significantly in the remote phase [5, 6], and those with giant CAA have a higher incidence of thrombosis and more pronounced intimal thickening, leading to coronary stenosis, myocardial infarction, and sudden death in severe cases [7–13]. In addition, the incidence of adverse cardiac events was significantly higher in KD patients with ≥ 6 -week CAAs than those with < 6-week CAAs (15% versus 0.2%) [14]. Even if the long-term prognosis of KD is closely related to the magnitude and duration of the CAA, a small or

regressed aneurysm can cause additional damage to the vascular tissue secondary to a persistent abnormality. Several scoring systems, such as the Harada, Kobayashi, and Egami [15–17] scores, have been established to screen KD patients with a higher risk for CAA; however, geographical variation and ethnicity limit the widespread use of these clinical assessment tools. Moreover, a few studies on medium-large CAA in KD have been reported. The present study aimed to determine the potential risk factors associated with medium-large CAA after acute KD.

Materials And Methods

1.1 Study design and population

We retrospectively reviewed the clinical records of consecutive children with KD treated between January 2013 and August 2021 at the Pediatrics of First Affiliated Hospital of Guangxi Medical University, China. The criteria for the diagnosis of KD were as follows: diagnosis of KD, compliant with the Diagnostic Guidelines for Kawasaki Disease (sixth revision, issued by the Japan Kawasaki Disease Research Committee in 2020) [18], and CAA, was defined as a z-score adjusted for body surface area (BSA) for a coronary artery internal diameter of ≥ 2.5 after 1 month of the disease course according to the guidelines on the diagnosis and management of cardiovascular sequelae in KD (JCS/JSCS 2020). CAA was classified based on the following z-scores: small aneurysm, 2.5 to < 5 ; moderate aneurysm, 5 to < 10 ; and large or giant aneurysm, ≥ 10 or internal diameter of ≥ 8 mm [19]. Children were excluded if they received treatment after the first 10 days of the onset of fever and the diagnosis of KD was unclear, received IVIG or hormone therapy outside the hospital, or if the data required for statistical analyses were incomplete.

All patients were first classified according to the z-score of coronary artery internal diameter into two groups: the medium-large CAA group ($n=20$) and small-sized CAA group ($n=70$). Patients received IVIG (2 g/kg per 24 hours) and oral aspirin (30–50 mg/kg per day) until the resolution of their fever for at least 72 hours. They subsequently received aspirin (3–5 mg/kg per day) until regression of the CAL was observed on two-dimensional (2D) echocardiography or all signs of inflammation had resolved. Patients were classified as IVIG resistant if they had a persistent or recrudescent fever (temperature, > 38.0 °C) for at least 36 hours but not longer than 7 days after receiving the initial IVIG infusion (2 g/kg). These patients received additional rescue treatment, such as the second dose of IVIG and steroid (e.g., prednisone or methylprednisolone) therapy.

1.2 Data collection

The following clinical and laboratory data were collected from the medical charts of the patients enrolled in this study and were reviewed using a standardized form: (1) general demographic data: age, gender, height, weight, and BMI; (2) clinical manifestations: duration of fever before admission, pediatric sequential organ failure assessment (pSOFA) score and Harada risk score on the day of admission, illness day at treatment (illness day 1 was considered the first day of fever), response to IVIG therapy,

incidence of incomplete KD, administration of steroid therapy, and the incidence of thrombosis; and (3) laboratory indicators: the highest value was selected for analysis in the case of the white blood cell count (WBC), neutrophil count, eosinophil count, aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, total serum bilirubin (TSB) level, and C-reactive protein (CRP) level; the lowest value was selected for the lymphocyte count, hemoglobin concentration, hematocrit, platelet count, serum albumin concentration, serum globulin concentration and serum sodium concentration. All the laboratory indicators were collected for assessment during the acute febrile period and before initial IVIG treatment. We calculated the neutrophil-to-lymphocyte count ratio, platelet-to-lymphocyte count ratio, lymphocyte-to-eosinophil count ratio, AST-to-ALT ratio (AST/ALT ratio), albumin-to-globulin ratio (A/G ratio), and CRP-to-albumin ratio (CRP/ALB ratio) based on the indicators mentioned above; (4) we also collected data on the coronary arterial internal diameters of the right coronary artery, left main coronary artery, left anterior descending artery, and left circumflex coronary artery from echocardiograms obtained at baseline (days < 10), week 2 (days 10–14), week 4 (days 20–50), and month 3 (days 80–100) after the onset of fever, and the z-score of the coronary artery corrected for the BSA was determined and recorded.

1.3 Statistical analysis

Normality of distribution was verified using the Shapiro–Wilk and homogeneity tests. Measurement of data with a normal distribution was expressed as mean $\pm$ standard deviation, and the two-independent sample t-test was used to compare data between the groups. Measurement data that did not have a normal distribution were expressed as the median (four-digit interval) [P_{50} (P_{25} , P_{75})], and these data were compared between the groups using the Mann–Whitney U test. Enumeration data were expressed as a percentage (%). The chi-square or Pearson chi-square test was used to perform intergroup comparisons. Binary logistic regression analysis (stepwise backward method) was used to analyze risk factors statistically, and the best threshold for the significant parameter was constructed using receiver operating characteristic (ROC) curves. Statistical correlations were determined by Spearman's correlation test, and two-tailed *P*-values were considered statistically significant if *P* was < 0.05. Statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA).

Results

2.1 Baseline characteristics

During the observation period, 353 children were enrolled in this study. Of these, 90 (25.6%) children had CAA, including 15 with medium-sized and 5 with large-sized CAAs. The mean age of the medium-large CAA group was 37 months (range 3–158 months). The male-to-female ratio of children in the medium-large CAA group was 3:1 (15 boys and 5 girls), with a ratio of incomplete KD of 0.54:1 (7/13); there were 6 cases (30%) of patients with IVIG resistance and 9 cases (45%) who had thrombosis. The mean age of the small-sized CAA group was 23 months (range 2–152 months). The male-to-female ratio of children in the small-sized CAA group was 2.9:1 (52 boys and 18 girls), with a ratio of incomplete KD of 0.49:1

(23/47); there were 14 cases (20%) of patients with IVIG resistance and 2 cases (2.9%) who had thrombosis. No deaths occurred in either group.

2.2 Comparison between the medium-large and small-sized CAA groups to analyze the risk factors for KD with medium-large CAA

2.2.1 Comparison Of Clinical Characteristics

The sum of the Harada risk scores and the incidence of thrombosis was higher in the medium-large CAA group than those in the small-sized CAA group, with a significant difference in both groups ($P < 0.05$). However, there were no statistically significant differences between the groups in terms of age, gender, height, weight, BMI, pSOFA score, fever duration before admission, days of illness at primary treatment, incidence of incomplete KD, and IVIG resistance or steroid therapy (all, $P > 0.05$), as shown in Table 1.

Table 1
Comparison of the clinical characteristics between medium-large and small-sized CAA groups

	Total (n=90)	medium-large CAA group (n=20)	small-sized CAA group (n=70)	<i>P</i>
Age [month, $P_{50}(P_{25}, P_{75})$]	16.50 (9.00, 31.25)	16.50 (8.00, 57.50)	16.50 (9.75, 29.00)	0.563
<12 months[n(%)]	12(13.3)	3(15.0)	9(12.9)	1.000
Male[n(%)]	67(74.4)	15(75.0)	52(74.3)	1.000
Height [m, $P_{50}(P_{25}, P_{75})$]	0.80 (0.71, 0.92)	0.82 (0.71, 1.05)	0.79 (0.72, 0.91)	0.446
Weight [kg, $P_{50}(P_{25}, P_{75})$]	10.00 (8.50, 13.50)	10.50 (8.35, 15.88)	10.00 (8.50, 12.93)	0.387
BMI [kg/m ² , $P_{50}(P_{25}, P_{75})$]	15.89±1.73	16.06±1.86	15.85±1.71	0.631
pSOFA score (point, mean ± SD)	0.67±1.57	0.80±2.46	0.63±1.23	0.670
Harada score (point, mean ± SD)	4.10±1.59	4.85±1.53	3.89±1.56	0.016
Fever duration before admission (day, mean ± SD)	8.83±5.22	9.30±6.17	8.70±4.96	0.653
Days of illness at primary treatment [day, mean ± SD]	10.27±5.44	10.45±5.77	10.22±5.38	0.871
Incomplete KD[n(%)]	30(33.3)	7(35.0)	23(32.9)	0.858
IVIG resistance[n(%)]	20(22.2)	6(30.0)	14(20.0)	0.520
Steroid therapy[n(%)]	9(10.0)	3(15.0)	6(8.6)	0.673

CAA, coronary artery aneurysm; IVIG, intravenous immunoglobulin; KD, Kawasaki disease; BMI, body mass index; pSOFA, pediatric sequential organ failure assessment.

	Total (n=90)	medium-large CAA group (n=20)	small-sized CAA group (n=70)	<i>P</i>
Thrombosis[n(%)]	11(12.2)	9(45.0)	2(2.9)	<0.001
CAA, coronary artery aneurysm; IVIG, intravenous immunoglobulin; KD, Kawasaki disease; BMI, body mass index; pSOFA, pediatric sequential organ failure assessment.				

2.2.2 Comparison Of Laboratory Characteristics

The laboratory indices analysis results of the two groups of patients are shown in Table 2. The medium-large CAA group showed higher values in the serum globulin concentration, proportions of CRP > 40 mg/L, serum albumin level < 35 g/L, and lower A/G ratio values than the small-sized CAA group, and the differences were statistically significant ($P < 0.05$).

Table 2
Comparison of laboratory characteristics between medium-large and small-sized CAA groups

	Total (n=90)	medium-large CAA group (n=20)	small-sized CAA group (n=70)	<i>P</i>
White blood cell count ($\times 10^9/L$, mean $\pm$ SD)	15.59 $\pm$ 7.76	18.27 $\pm$ 9.80	14.83 $\pm$ 6.97	0.081
>12 $\times 10^9/L$ [n(%)]	57(63.3)	14(70.0)	43(61.4)	0.483
Neutrophils count ($\times 10^9/L$, mean $\pm$ SD)	9.62 $\pm$ 6.95	11.93 $\pm$ 8.40	8.96 $\pm$ 6.40	0.093
$\geq 80\%$ [n(%)]	12(13.3)	4(20.0)	8(11.4)	0.534
Lymphocytes count ($\times 10^9/L$, mean $\pm$ SD)	4.34 $\pm$ 2.82	4.54 $\pm$ 2.85	4.29 $\pm$ 2.83	0.732
NLR(mean $\pm$ SD)	3.45 $\pm$ 3.72	4.41 $\pm$ 4.79	3.18 $\pm$ 3.35	0.195
LER(mean $\pm$ SD)	59.28 $\pm$ 123.89	56.54 $\pm$ 106.39	60.07 $\pm$ 128.28	0.911
Hemoglobin (g/L, mean $\pm$ SD)	103.80 $\pm$ 15.73	99.91 $\pm$ 16.73	104.91 $\pm$ 15.37	0.211
$\leq 110g/L$ [n(%)]	56(62.2)	14(70.0)	42(60.0)	0.416
Hematocrit(mean $\pm$ SD)	0.31 $\pm$ 0.05	0.30 $\pm$ 0.05	0.32 $\pm$ 0.04	0.266
<0.35[n(%)]	71(78.9)	16(80.0)	55(78.6)	1.000
Platelet count [$\times 10^{12}/L$, $P_{50}(P_{25}, P_{75})$]	364.60 (253.83,499.30)	408.00 (272.00,637.43)	354.50 (245.25,460.75)	0.220
>350 $\times 10^{12}/L$ [n(%)]	46(51.1)	11(55.0)	35(50.0)	0.693
PLR(mean $\pm$ SD)	119.73 $\pm$ 83.13	124.71 $\pm$ 77.29	118.31 $\pm$ 85.20	0.763
CRP(mg/L, mean $\pm$ SD)	76.23 $\pm$ 58.81	93.69 $\pm$ 54.31	71.25 $\pm$ 59.46	0.133
>40mg/L[n(%)]	58(64.4)	17(85.0)	41(58.6)	0.029

CAA, coronary artery aneurysm; NLR, neutrophil count-to-lymphocyte count ratio; LER, lymphocyte count-to-eosinophil count ratio; PLR, platelet count-to-lymphocyte count ratio; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; A/G ratio, albumin-to-globulin ratio.

	Total (n=90)	medium-large CAA group (n=20)	small-sized CAA group (n=70)	<i>P</i>
Sodium(mmol/L, mean ± SD)	136.29±3.12	135.43±3.33	136.53±3.04	0.166
≤133mmol/L[n(%)]	11(12.2)	4(20.0)	7(10.0)	0.414
ALT(U/L, mean ± SD)	55.58±54.99	67.86±65.78	52.08±51.50	0.260
AST(U/L, mean ± SD)	56.64±74.76	56.33±67.93	56.73±77.06	0.983
AST/ALT ratio(mean ± SD)	1.37±0.96	1.26±1.23	1.40±0.87	0.580
Total bilirubin (umol/L, mean ± SD)	8.90±14.43	11.14±15.98	8.26±14.01	0.433
Albumin(g/L, mean ± SD)	35.33±5.71	33.74±5.37	36.05±5.74	0.111
<35g/L[n(%)]	43(47.8)	14(70.0)	29(41.4)	0.024
Globulin(g/L, mean ± SD)	27.46±9.07	31.70±10.76	26.25±8.22	0.017
A/G ratio(mean ± SD)	1.44±0.56	1.17±0.45	1.52±0.57	0.014
CRP/ALB ratio(mean ± SD)	2.30±1.91	2.89±1.90	2.13±1.89	0.120
CAA, coronary artery aneurysm; NLR, neutrophil count-to-lymphocyte count ratio; LER, lymphocyte count-to-eosinophil count ratio; PLR, platelet count-to-lymphocyte count ratio; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; A/G ratio, albumin-to-globulin ratio.				

2.2.3 Analysis of risk factors for KD with medium-large CAA

Univariate analysis identified five indices that were significantly associated with medium-large CAA development: the Harada risk score, serum globulin level, A/G ratio values, CRP level > 40 mg/L, and serum albumin level < 35 g/L. The Harada risk score was excluded from the multivariate analysis because the variables included in this score, such as CRP > 40 mg/L and serum albumin level < 35 g/L, were included in the multivariable model and all other variables included in this score were not statistically significant on univariable analysis, such as male sex, < 1 year of age, WBC > 12·10⁹/L, platelet count > 350·10¹²/L, or hematocrit <0.35. The A/G ratio, calculated as the serum albumin level divided by serum globulin level, was included in the multivariable analysis instead of the two separate indicators. Ultimately, the values of A/G ratio, CRP level > 40 mg/L, and serum albumin level < 35 g/L were entered into the binary logistic regression analysis, which revealed that the A/G ratio was the only significant independent predictor of medium-large CAA in KD, and the risk for the formation of medium-

large CAA increased by 2.503 times for every unit of increase ($P = 0.039$, 95% confidence interval [95% CI] 1.068–11.492).

2.3 Predictive role of A/G ratio in KD with medium-large CAA

Binary logistic regression analysis showed that a low A/G ratio value was significantly associated with medium-large CAA. The area under the ROC curve for the value of A/G ratio was 0.684 (95% CI: 0.558–0.810), and the sensitivity and specificity for predicting medium-large CAA in KD patients were 80% and 59%, respectively, at a cutoff point of 1.35 (Fig. 1). In addition, after 1 month of the disease course, the A/G ratio was negatively correlated with the internal diameter of the left main coronary artery ($r = -0.407$, $P < 0.001$). However, there was no correlation between the A/G ratio and the internal diameter of the right coronary artery ($r = -0.212$, $P = 0.053$) (Fig. 2A). The same results were found when the A/G ratio was compared with the z-score of coronary artery internal diameter ($r = -0.247$, $P = 0.023$ for the left main coronary artery and $r = -0.078$, $P = 0.480$ for the right coronary artery) (Fig. 2B). Among the 82 patients whose data for coronary outcome were complete from baseline at weeks 2, 4, and 3 months, coronary artery regression was observed after 1 month of the disease course and the right coronary artery showed early regression (after 2 weeks of onset) in 39 of 82 (47.6%) patients with an A/G ratio of < 1.35 (Fig. 3). The change of the left main coronary artery was significantly larger in patients with an A/G ratio of < 1.35 at month 1 (Fig. 3A and 3C). However, the change in the right coronary artery was not significantly greater at month 1 (Fig. 3B and 3D).

Discussion

This retrospective study evaluated the potential risk factors associated with medium-large CAA identified after acute KD. In this study, thrombosis was significantly more frequent in patients with KD with medium-large CAA than those with small-sized CAA. In the KD group, we found that the A/G ratio alone was highly associated with medium-large CAA, which was negatively correlated with the internal diameter of the left main coronary artery after 1 month of the disease course.

The development of CAA is the most severe complication of KD, among them, cardiac sequelae caused by medium-large CAA are associated with severe morbidity in pediatric patients. In our study, the CAA incidence was 25.5%, where the incidence of medium-large CAA is 5.7%, which was higher than that reported in the literature[4]. This may be because many previously reported studies used Japanese Ministry of Health established criteria for coronary abnormalities, which has been recognized to underdiagnose of the true prevalence of lesions. In addition, a substantial number of patients with severe KD or those with failed medical treatment was referred to our hospital.

Of note, identifying risk factors that provide early warning signs for susceptibility to develop medium-large CAA in children with KD is clinically important. In the current study, we found that a lower A/G ratio, which may be explained by hypoalbuminemia and/or hyperglobulinemia, served as an independent predictor of medium-large CAA and had a sensitivity of 80% and a specificity of 59% at a cutoff value of < 1.35 . Hypoalbuminemia is an efficient predictor of IVIG resistance and CAA formation [18, 20–25]. This

is consistent with our findings that serum albumin levels of < 35 g/L were significantly increased in KD patients with medium-large CAA. Interestingly, the same results were also found in serum globulin levels. However, neither albumin nor globulin, the A/G ratio was the only risk factor associated with medium-large CAA in the multivariate analysis. These results are in line with previous studies on hepatic dysfunction secondary to KD, stating that the A/G ratio served as an independent predictor of CAA at a cutoff value of < 1.48 [26]. Similarly, our results indicate that a lower A/G ratio indicates a greater risk for CAA development since our study found that the risk of KD complicated with medium-large CAA increases when $A/G < 1.35$, unlike previous studies. Future studies on KD should analyze the effect of the A/G ratio on CAA development.

Based on the above findings, we also found that the A/G ratio was negatively correlated with the internal diameter of the left main coronary artery, and there was no correlation between the A/G ratio and the internal diameter of the right coronary artery. Further analysis revealed that patients were divided into two groups based on an A/G ratio value of 1.35 as the cutoff value and the dynamic change of the internal diameter of the coronary artery. Notably, in the group with an A/G ratio of < 1.35 , the coronary artery internal diameter was larger than that in the group with an A/G ratio of ≥ 1.35 within 3 months of disease onset. Regression of coronary artery was noted after 1 month of the disease course in both groups and the right coronary artery showed earlier regression, which was consistent with a previous study [27]. In our study, we also found that the extent of the expansion of the left main coronary artery was consequently significantly more prominent in the patients with A/G ratio of < 1.35 at 1 month after onset, which is contrary to the results of Mammadov et al. [26], who suggested that A/G ratio was negatively correlated with the internal diameter of the right coronary artery. The possible reason for this may be differences in study populations leading to varying outcomes. Unlike the earlier study, including patients with KD patients with and without CAA, the present study was carried out only on KD patients with CAA. Furthermore, the inconsistencies among the regression time between the left and right coronary arteries may also contribute to the discrepancy in the results. Thus, more in-depth research is needed to resolve these inconsistencies.

The Harada score, a risk scoring system for KD, has been exhaustively evaluated to predict children at a higher risk for the development of CAA with a sensitivity of 90% and specificity of 51% [17]. In this study, larger CAAs have an associated higher Harada risk scores, but only CRP level was greater than 40 mg/L, and serum albumin level was lower than 35 g/L, suggesting that these values, included in the risk score, were statistically significant. Previous studies have also proposed high CRP and low serum albumin levels as predictors of CAA in children diagnosed with KD [16, 28–30], and recent studies found that the CRP-to-albumin ratio (CRP/ALB ratio) can serve as a novel predictive marker for CAA formation and IVIG resistance in patients with KD [31, 32]. While the present study also found a higher CRP/ALB ratio in the medium-large CAA group than the small-sized CAA group, the difference was not significant. Therefore, further multicenter studies are needed to validate the predictive accuracy of this parameter.

There are some limitations of this study. Firstly, this was a single-center retrospective study and is susceptible to selection bias. Secondly, the sample size of this study was underpowered to conduct a

highly informative multivariate analysis. Nevertheless, the binary logistic regression analysis revealed that a low A/G ratio was highly significantly related to a higher likelihood of medium-large CAA development in children diagnosed with KD. Further studies with a larger sample size are needed to confirm the finding. Third, since a significant amount of data were missing for some parameters, the levels of serum procalcitonin, interleukin-6, and brain natriuretic peptide were not analyzed in this study. Therefore, prospective clinical large cohort trials are warranted.

Conclusion

A lower A/G ratio is an independent predictor of medium-large CAA development in children diagnosed with KD. Medium-large CAA have greater odds of developing thrombosis. Thus, close monitoring with frequent echocardiography is needed for these patients.

Abbreviations

ALT

alanine aminotransferase

AST

aspartate aminotransferase

BMI

body mass index

BSA

body surface area

CAA

Coronary artery aneurysms

CAL

coronary artery lesions

CRP

C-reactive protein

CI

confidence interval

IVIG

intravenous immunoglobulin

KD

Kawasaki Disease

OR

odds ratios

pSOFA

pediatric sequential organ failure assessment

ROC

receiver operating characteristic
TSB
total serum bilirubin
Wald
wald test statistics
WBC
white blood cell count
2D
two-dimensional

Declarations

Ethics approval and consent to participate: Approval for this research was required from the Medical Ethics Committee of the First Affiliated Hospital of GuangXi Medical University(Code number; 2021(KY-E-240)). Informed consent was obtained from the parents of each patient.

Consent for publication: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Availability of data and materials: The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

Competing interests: All authors declare that they have no conflicts of interests.

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Authors' contributions: LJ drafted the manuscript, contributed to the data collection, performed the statistical analysis, and approved the final manuscript as submitted. SDY provided Figures, contributed to the data collection, study design, and approved the final manuscript as submitted. YBB contributed to the data collection and approved the final manuscript as submitted. QSY provided primary treatment to these patients while they were admitted, and contributed to the study design. CC prepared the tables, contributed to the data collection, and approved the final manuscript as submitted. PYS conceived and designed the study, contributed to the data collection, and approved the final manuscript as submitted.

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Figures

Figure 1

The predictive role of albumin-to-globulin (A/G) ratio in medium-large CAA. When the A/G ratio was substituted in a ROC curve analysis, the area under the receiver operating characteristic curve (AUC) was 0.684. The estimated sensitivity of the A/G ratio for medium-large CAA was 80%, and specificity was 59%, with a cutoff of A/G ratio 1.35.

Figure 2

Spearman's correlation analysis between albumin-to-globulin (A/G) ratio and coronary artery outcome. After 1 month of the disease course, A/G ratio was negatively correlated with the internal diameter of the left main coronary artery ($r = -0.407$, $p < 0.001$). However, there was no correlation between the A/G ratio and the internal diameter of the right coronary artery ($r = -0.212$, $p = 0.053$) (A). The same results were found when the A/G ratio was compared with the z-score of coronary artery internal diameter ($r = -0.247$, $p = 0.023$ for left main coronary artery and $r = -0.078$, $p = 0.480$ for right coronary artery, respectively) (B).

Figure 3