Cardiology in the Young

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Using nomogram scores to predict the early regression of coronary artery aneurysms of Kawasaki disease

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Original Article

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Abstract

Background: Coronary artery aneurysms have been considered the most serious complication of Kawasaki disease. However, some coronary artery aneurysms do regress. Therefore, the ability to predict the expected time of coronary artery aneurysm regression is critical. Herein, we have created a nomogram prediction system to determine the early regression (<1 month) among patients with small to medium coronary artery aneurysms. *Methods:* Seventy-six Kawasaki disease patients identified with coronary artery aneurysms during the acute or subacute phase were included. All the patients who met inclusion criteria demonstrated regression of coronary artery aneurysms within the first-year post Kawasaki disease diagnosis. The clinical and laboratory parameters were compared between the groups of coronary artery aneurysms regression duration within and beyond 1 month. Multivariate logistic regression analysis was used to identify the independent parameters for early regression based on the results from the univariable analysis. Then nomogram prediction systems were established with associated receiver operating characteristic curves. *Results:* Among the 76 included patients, 40 cases recovered within 1 month. Haemoglobin, globulin, activated partial thromboplastin time, the number of lesions, location of the aneurysm, and coronary artery aneurysm size were identified as independent factors for early regression of coronary artery aneurysms in Kawasaki disease patients. The predictive nomogram models revealed a high efficacy in predicting early regression of coronary artery aneurysms. *Conclusion:* The size of coronary artery aneurysms, the number of lesions, and the location of aneurysms presented better predictive value for predicting coronary artery aneurysms regression. The nomogram system created from the identified risk factors successfully predicted early coronary artery aneurysm regression.

Introduction

Coronary artery aneurysms have been observed as one of the dominant adverse complications associated with Kawasaki disease.[1] Coronary artery aneurysms are identified in 4.5% of Kawasaki disease patients during the acute phase, even if such patients received timely intravenous immunoglobulin administration.[2] Usually, small-size coronary artery aneurysms can completely regress. However, 50–67% of medium-sized coronary artery aneurysms would persist, and 14–20% would progress to stenosis due to the malformation of coronary morphology.[3–6] If coronary artery aneurysms remain for more than 1 month, it is considered the sequelae of Kawasaki disease. Furthermore, the severity of coronary artery aneurysms after 1 month from disease onset is usually based on the dilation of coronary artery aneurysms, which are classified into the following five categories. I. No dilation group. II. Transient dilation group in the acute phase. III. Regression group. IV. Remaining coronary aneurysm group. V. Coronary stenosis lesion group. Moreover, the long-term assessment and management strategy of patients with coronary artery aneurysm sequelae is individual according to the corresponding severity stratification. Thus, assessing the regression time of small to medium coronary artery aneurysms is essential and could benefit from follow-up.[7] Currently, particular efforts have been made to build systems to predict persistent or regressed coronary artery aneurysms. However, there is no available research to determine any potential risk factors in distinguishing early (within 1 month) and delayed (beyond 1 month) regression, which would much impact the management strategy.

In clinical practice, it is urgent to get a practical tool to predict the development and prognosis of coronary artery aneurysms in Kawasaki disease, as such patients might significantly benefit from personalised management. Some studies have investigated the risk factors for coronary artery aneurysm development and persistence, proposing several risk-scoring systems.[8–11] Moreover, to the best of our knowledge, there are few studies focusing on predicting

the coronary artery aneurysms regression,[12,13] especially within the first month from Kawasaki disease onset using the nomogram scores, which is a valuable tool for predicting the prognosis of different diseases[14,15] and could perform much better than previous models.[16,17] Nomogram scores may become a promising candidate for coronary artery aneurysm regression prediction in Kawasaki disease. The early regression of coronary artery aneurysms could help to modify the follow-up strategy of Kawasaki disease, which would benefit the total cost of Kawasaki disease. Therefore, early detection of risk factors can be a great advantage.

Herein, this study aimed to identify the parameters associated with the early coronary artery aneurysms regression within the first month of Kawasaki disease and propose a nomogram model for predicting coronary artery aneurysms regression in the Kawasaki disease population for the first time.

Methods

Patient population

All patients were enrolled for this analysis from January 2016 to December 2020 in West China Second University Hospital, Sichuan University, a single-centre, prospective observational research. The minimal follow-up duration was 1 year. This research strictly followed the STROBE statement and was approved by the Ethics Committee of the West China Second Hospital of Sichuan University (approval number 2014-034). Informed written consent was obtained from the parents after the nature of this study had been fully explained to them. All questionnaires were pretested and revised accordingly. Two pre-trained individual physicians conducted data collection and follow-up. Any related questionnaires were double-checked to assure accuracy. All the clinical data were both confirmed by electronic medical records and owned follow-up databases.

Inclusion and exclusion criteria

We used the following inclusion criteria to recruit candidates for further analysis: All the patients should meet the diagnostic criteria for complete or incomplete diagnostic standards recommended by the Japanese Circulation Society (2013) for diagnosis, treatment, and long-term management of Kawasaki disease, and two physicians should confirm the diagnosis; Echocardiography identified coronary artery aneurysms during the acute or subacute phase, and all coronary artery aneurysms recovered within the first year during follow-up; Programmed questionnaires, basic essential information, clinical manifestation, results of haematological examinations, therapeutic procedure, echocardiography results, and follow-up outcomes were well collected; The baseline haematological examinations were completed in the acute phase of Kawasaki disease before intravenous immunoglobulin administration; The age of included patients varied from 2 years to 6 years, the most popular age for Kawasaki disease onset, to easily balance the bias from high-risk ages; The characteristics of coronary arteries were evaluated either by transthoracic echocardiography or transcatheter angiography; Relapsed Kawasaki disease was defined as a repeat episode of complete or incomplete Kawasaki disease after complete resolution of the previous episode; If the patients were diagnosed as relapsed Kawasaki disease, they should be free from any coronary artery lesions in their prior Kawasaki disease episode. The exclusion criteria included the following: Patients demonstrated any cardiovascular malformation; Patients had been diagnosed with an autoimmune disease before Kawasaki disease onset; Patients had received anticoagulant or antiplatelet medication before Kawasaki disease onset; Patients underwent any cardiac surgery; Myocarditis had been suspected before Kawasaki disease; Glucocorticoids had been provided before intravenous immunoglobulin administration; The monoclonal antibody was provided, including tumour necrosis factor-α or interleukin-6 antibodies; Macrophage activation syndrome, or hemophagocytic lymphohistiocytosis, was diagnosed due to Kawasaki disease; No available echocardiographic record could be addressed for ≥1 year; The recurrent relapsed Kawasaki disease patients (≥2 times) should be excluded.

Therapeutic and follow-up procedures

All patients with Kawasaki disease were treated with high-dose intravenous immunoglobulin (2 g/kg given as a single intravenous infusion) combined with 30–50 mg/kg/day high-dose aspirin. Those with recrudescent or persistent fever for ≥36 hours after the first intravenous immunoglobulin infusion were treated with a second dose of 2 g/kg intravenous immunoglobulin. Methylprednisolone (30 mg/kg/day for 3 consecutive days) followed by oral prednisone tapered over 7 days would be considered after the second intravenous immunoglobulin administration. The first day of fever was defined as the first day of illness onset. Intravenous immunoglobulin resistance was defined as persistent or recurrent fever (temperature of ≥38.0°C orally) or other clinical signs of Kawasaki disease for at least 36 hours but not >7 days after the initial intravenous immunoglobulin. The patients were discharged from the hospital after their temperature remained normal for >48 hours and haematological examination returned to average values. Follow-up was started at hospital discharge, and all the involved patients were required to revisit the hospital for echocardiographic evaluations at 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months, which was documented from the end of the subacute phase. The coronary artery aneurysms, which regressed within 1 month, were considered early regression, while the lesions recovered after 1 month was considered delayed regression.

Echocardiographic evaluation

Two well-trained paediatric physicians performed all echocardiographs. The physicians examining enrolled patients were blinded to the clinical manifestation of receivers. The first echocardiography was performed before intravenous immunoglobulin administration. The second echocardiography was performed during the subacute phase or before hospital discharge. We defined the morphology and lumen dilation of the coronary artery as the most severe condition between acute and subacute phases of Kawasaki disease, which were documented as aneurysm size in the research. At least two echocardiographic evaluations were completed to match the minimal requirement for the first-month follow-up. We defined the first time from observing the pre-existed coronary artery aneurysms to its recovery into average size as the time for recovery. A coronary artery aneurysm was defined according to the criteria of the Japanese Circulation Society as a coronary artery branch internal lumen diameter of >3 mm in a child aged <5 years and an artery of >4 mm in a child aged ≥5 years, or when an arterial segment was 1.5 times than its adjacent segment. The coronary artery aneurysms were classified as small aneurysms (localised dilatation with ≤4 mm internal diameter), medium aneurysms (aneurysms with an internal diameter from >4 to <8 mm), and giant aneurysms (aneurysms with an internal diameter of ≥8 mm). In this study, the size of the coronary artery

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lesion was defined as the largest one within the acute phase of Kawasaki disease. Besides, the number of injuries on coronary artery branches had also been included for further analysis.

Risk factor analysis

At first, the enrolled patients' essential clinical characteristics and haematological examination results were recorded, and all the parameters are listed in Table 1 and Supplementary Table 1. Then, univariate analysis was performed between the patients with coronary artery aneurysm recovery within 1 month and those beyond 1 month. Thus, the regression of the coronary artery aneurysm indicated the total recovery to standard size from a recorded coronary artery aneurysm. Then, the multivariable analysis was completed using logistic regression to identify the independent factors among the significant results according to univariable analysis. Then, nomograms were formulated based on the results of the univariate and multivariable analyses. We selected the final prognostic nomogram model using a backward step-down selection process with the Akaike information criterion. Afterward, receiver operating characteristic curves were used to identify the predictive value of the risk factors and monogram scores found by comparison. Lastly, decision curve analysis was conducted to evaluate the efficacy of nomogram prediction.

Statistical analysis

Data analysis was conducted using SPSS 22.0 (SPSS Inc. Chicago, Illinois, United States of America). Quantitative data were presented as the mean ± standard deviation and median with range, while qualitative data were expressed as n. Differences between the two groups were assessed using the independent t-test or Mann–Whitney U test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables. The predictive validity of candidate risk factors for coronary artery aneurysm recovery within the first month after the subacute phase was determined by receiver operating characteristic curve analysis. P values of <0.05 defined statistical significance. Nomograms and decision curve analysis were formulated and conducted using the *rms* and *rmda* packages of R version 3.3.2 (http://www.r-project.org).

Results

Study population

A total of 127 patients with observed coronary artery aneurysms in acute and subacute phases were included in this research. Additionally, 76 patients were finally selected for further analysis by fully addressing our inclusion and exclusion criteria. There were 21 patients who presented neurological symptoms, most of them complained of headaches, and only one suffered from aseptic meningitis. Forty patients were diagnosed with incomplete Kawasaki disease. While 19 patients demonstrated intravenous immunoglobulin resistance, we recorded 29 relapsed cases. Thirty-six patients demonstrated the existence of coronary artery aneurysms after 1 month, considered delayed regression, while 40 patients presented with coronary artery aneurysm regression within 1 month, identified as early regression.

Risk factors related to persistent coronary artery aneurysms within 3 weeks

As shown in Table 1, the univariable analysis revealed several parameters associated with the early coronary artery aneurysms regression, including haemoglobin ($p = 0.031$), globulin ($p = 0.0014$), K^+ ($p = 0.028$), activated partial thromboplastin time ($p = 0.000$), numbers of coronary artery aneurysms lesions ($p = 0.007$), location of the aneurysm ($p = 0.035$), and aneurysm size ($p = 0.001$). Then, we put such parameters into logistic regression for multivariable analysis. Then, six parameters were identified as independent factors for early coronary artery aneurysms regression (Table 2): haemoglobin (odds ratio [OR] = 0.935, $p = 0.000$, 95% confidence interval [CI] 0.902–0.969), globulin (OR = 0.921, $p = 0.010$, 95% CI 0.865–0.981), activated partial thromboplastin time (OR = 1.317, $p = 0.000$, 95% CI 1.223–1.419), numbers of coronary artery aneurysm lesions (OR = 41.004, $p = 0.000$, 95% CI 9.749–172.456), location of the aneurysm (OR = 2.129, $p = 0.002$, 95% CI 1.305–3.474), and aneurysm size (OR = 70.875, $p = 0.000$, 95% CI 15.660–322.001). Besides, all the involved factors for univariable analysis are presented as the median with a range in Supplementary Table 1.

Nomogram calculation

Nomogram prediction was made according to the univariable and multivariable analysis results. The nomogram formulas are presented in Figure 1 based on the seven identified parameters in univariable analysis and Figure 2 based on the six multivariable analysis-targeted independent risk factors. Using the established nomogram formula, we calculated every enrolled nomogram score of univariable factors (Uni_nomo), and the average scores of Uni_nomo were 119.01 ± 19.27 among early regression patients and 174.69 ± 41.67 among delayed regression patients. We calculated multivariable factors (Multi_nomo), and the average scores of Multi_nomo were 119.11 ± 19.87 among early regression patients and 174.42 ± 41.57 among delayed regression patients.

Receiver operating characteristic and decision curve analysis evaluations

Receiver operating characteristic curves were included to validate independent factors' efficacy and nomogram scores in predicting early coronary artery aneurysms regression. However, aneurysm size alone (area under the curve = 0.712, standard error = 0.059, 95% CI 0.597–0.827) demonstrated an intermit efficacy in distinguishing coronary artery aneurysms regression within 1 month, while the receiver operating characteristic curve of Uni_nomo (area under the curve = 0.941, SE = 0.027, 95% CI 0.887–0.995) and Multi_nomo (area under the curve = 0.939, SE = 0.028, 95% CI 0.884–0.993) scores presented an excellent efficacy in detecting coronary artery aneurysms regression (Fig 3). Lastly, the decision curve analysis was recruited to assess the advantages of nomogram scores. The decision curve analysis was performed based on the estimated incidence of coronary artery aneurysms of around 10% among all Kawasaki disease patients. The Uni_nomo and Multi_nomo scores revealed the same advantage in distinguishing coronary artery aneurysms that recovered within 1 month among most of the range of the high-risk threshold (Fig 4).

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Table 1. Univariate analysis for factors of early coronary artery aneurysm regression.

Variables	Early coronary artery aneurysms regression (n = 40)	Delayed coronary artery aneurysms regression (n = 36)	Sig.
Gender			
Female	8 (20.00%)	15 (41.77%)	0.071
Male	32 (80.00%)	21 (58.33%)	
Complications in CNS	15 (37.50%)	6 (16.67%)	0.077
Incomplete KD	23 (57.50%)	17 (47.22%)	0.491
Intravenous immunoglobulin resistance	9 (22.50%)	10 (27.78%)	0.608
Relapsed KD	18 (45.00%)	11 (30.56%)	0.366
White blood cell ($\times 10^9$/L)	14.52 ± 4.86	13.94 ± 5.37	0.623
Neutrophils (%)	65.80 ± 12.73	62.55 ± 15.22	0.331
Lymphocyte (%)	23.53 ± 10.53	27.43 ± 13.14	0.155
Ratio of neutrophils to lymphocyte	4.11 ± 4.67	3.15 ± 2.34	0.269
Monocyte (%)	10.67 ± 4.09	9.91 ± 4.08	0.420
Haemoglobin (g/L)	110.43 ± 11.51	104.47 ± 12.03	0.031*
Platelet ($\times 10^9$/L)	331.18 ± 113.25	375.44 ± 182.99	0.216
Ratio of platelet to lymphocyte	129.68 ± 91.59	120.50 ± 71.03	0.630
CRP (mg/L)	83.61 ± 53.35	91.50 ± 57.69	0.538
ESR (mm/h)	55.82 ± 24.07	64.00 ± 32.27	0.238
Alanine aminotransferase (ALT, U/l)	54.83 ± 66.68	61.36 ± 64.42	0.666
Aspartate aminotransferase (AST, U/l)	50.90 ± 55.89	49.61 ± 64.82	0.926
Ratio of AST to ALT	1.43 ± 0.80	1.12 ± 0.71	0.079
Total bilirubin (umol/L)	9.62 ± 10.59	9.09 ± 9.60	0.829
Direct bilirubin (DBIL, umol/L)	6.72 ± 8.96	5.20 ± 7.57	0.480
Indirect bilirubin (umol/L)	4.20 ± 3.46	4.21 ± 3.55	0.986
Albumin (ALB, g/L)	35.73 ± 7.52	35.70 ± 5.30	0.983
Globulin (GLB, g/L)	31.46 ± 6.28	27.78 ± 6.51	0.014*
Prealbumin (PA, g/L)	58.55 ± 43.33	65.31 ± 22.91	0.578
γ-Glutamyl transpeptidase (γGT, U/l)	89.80 ± 90.04	86.56 ± 96.93	0.880
Lactate dehydrogenase (LDH, U/L)	396.38 ± 186.24	364.69 ± 202.83	0.498
Urea nitrogen (UN, mmol/L)	3.46 ± 2.42	3.06 ± 0.97	0.386
Creatinine (Cr, umol/L)	30.35 ± 14.19	26.50 ± 7.59	0.178
Serum cystatin C (CysC, umol/L)	1.05 ± 0.59	0.975 ± 0.19	0.631
K+ (mmol/L)	4.12 ± 0.51	4.40 ± 0.58	0.028*
Na+ (mmol/L)	132.46 ± 20.75	137.33 ± 3.12	0.393
P- (mmol/L)	1.28 ± 0.28	1.39 ± 0.28	0.092
Cl- (mmol/L)	101.61 ± 3.94	103.24 ± 3.58	0.077
Ca2+ (mmol/L)	7.93 ± 33.78	2.28 ± 0.14	0.341
Mg2+ (mmol/L)	0.96 ± 0.17	0.90 ± 0.10	0.106
Total cholesterol (TC, mmol/L)	2.97 ± 0.52	3.07 ± 0.95	0.748
Triglyceride (TG, mmol/L)	1.37 ± 0.46	1.39 ± 0.54	0.932
HDL-C (mmol/L)	0.50 ± 0.13	0.51 ± 0.20	0.895
LDL-C (mmol/L)	2.14 ± 0.59	2.28 ± 0.92	0.654
Prothrombin time (s)	13.88 ± 3.48	14.23 ± 1.79	0.682

(*Continued*)

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Table 1. (*Continued*)

Variables	Early coronary artery aneurysms regression (n = 40)	Delayed coronary artery aneurysms regression (n = 36)	Sig.
Activated partial thromboplastin time (s)	32.64 ± 5.01	40.37 ± 6.67	0.000*
Fibrinogen (Fg, mg/dL)	562.15 ± 134.30	501.71 ± 156.42	0.193
D-dimer (mg/L)	1.72 ± 0.81	2.19 ± 1.73	0.405
CTnI (ug/L)	0.03 ± 0.06	0.02 ± 0.03	0.587
NT-BNP (pg/ml)	2384.15 ± 4416.91	2384.01 ± 4800.79	0.999
Cardiac enlargement	7 (17.50%)	6 (16.67%)	0.584
Valver regurgitation	10 (25.00%)	6 (16.67%)	0.273
Number of lesions			
1	38 (95.00%)	27 (75.00%)	0.007*
2	2 (5.00%)	7 (19.44%)	
3	0 (0.00%)	2 (5.56%)	
Location of aneurysm			
Left coronary artery	33 (82.50%)	25 (69.44%)	0.035*
Left anterior descending artery	3 (7.50%)	2 (5.56%)	
Left circumflex artery	0 (0.00%)	0 (0.00%)	
Right coronary artery	4 (10.00%)	9 (25.00%)	
Aneurysm size	3.30 ± 0.25	3.57 ± 0.40	0.001*

*$p < 0.05$

Table 2. Multivariate analysis for factors of early coronary artery aneurysm regression.

Variables	OR	Sig.	Lower 95% CI	Upper 95%CI
Haemoglobin	0.935	0.000	0.902	0.969
Globulin	0.921	0.010	0.865	0.981
K^+	1.586	0.200	0.783	3.212
Activated partial thromboplastin time	1.317	0.000	1.223	1.419
Number of lesions	41.004	0.000	9.749	172.456
Location of aneurysm	2.129	0.002	1.305	3.474
Aneurysm size	70.875	0.000	15.660	322.001

Discussion

Coronary artery aneurysms are considered the worst concern in patients with Kawasaki disease. Regarding pathologic mechanisms of coronary artery aneurysms regression, a prior study by Sasaguri et al.[18] demonstrated the remarkable intimal thickening with regenerated endothelium rather than the organisation of massive thrombus or calcification was related to the development and outcomes of coronary artery aneurysms. Mild and transient dilation of coronary arteries may recover within 4–6 weeks.[1] In this cohort, coronary artery aneurysm regression referred to the internal diameter of coronary arteries that returned to the standard size by echocardiographic measurements during the follow-up. Coronary artery aneurysm regression indicates a reduction of the maximum internal diameter of coronary artery aneurysms, and the injuries to the coronary artery wall might remain.[19] Therefore, regressed coronary artery aneurysms could also lead to the development of acute coronary syndrome in adults; however, it has a significantly low incidence.[20,21] Nevertheless, early coronary artery aneurysm regression would definitely benefit Kawasaki disease patients with a lower incidence of adverse long-term complications and shortened duration of medication administration.[22] According to previous studies, the coronary artery aneurysms regression was more likely to be observed in patients with smaller size coronary artery aneurysms. The degree of coronary artery lesions was one of the critical risk factors for coronary artery aneurysm regression. However, striking discrepancies exist among Kawasaki disease patients in the ratio, duration, and long-term prognosis of coronary artery aneurysms regression.[23] Thus, it was critical to establish a system for predicting the expected time for coronary artery regression.

In the past decade, many efforts have been made to identify the potential risk factors for coronary artery aneurysms formation, including age (<1 year or >9 years),[24,25] sex,[26] delayed intravenous immunoglobulin application,[26] intravenous immunoglobulin resistance,[27] increased inflammation activity,[26,28] cardiac injuries,[29] neutrophil-to-lymphocyte ratio,[28] hypoalbuminaemia, total bilirubin, platelet count, fever duration,[27] and tachycardia.[30] Based on the identified risk factors, a series of scoring systems for coronary artery aneurysm prediction were subsequently developed.[26] Unfortunately, a limited number of studies have investigated the factors determining coronary artery aneurysms regression.[23,31] Recently, Chen et al.[32] have revealed that the cases of coronary artery aneurysms with no calcification, smaller diameter, and younger age were more likely to regress. Furthermore, the diameter of 5.6 mm for predicting coronary artery aneurysms regression

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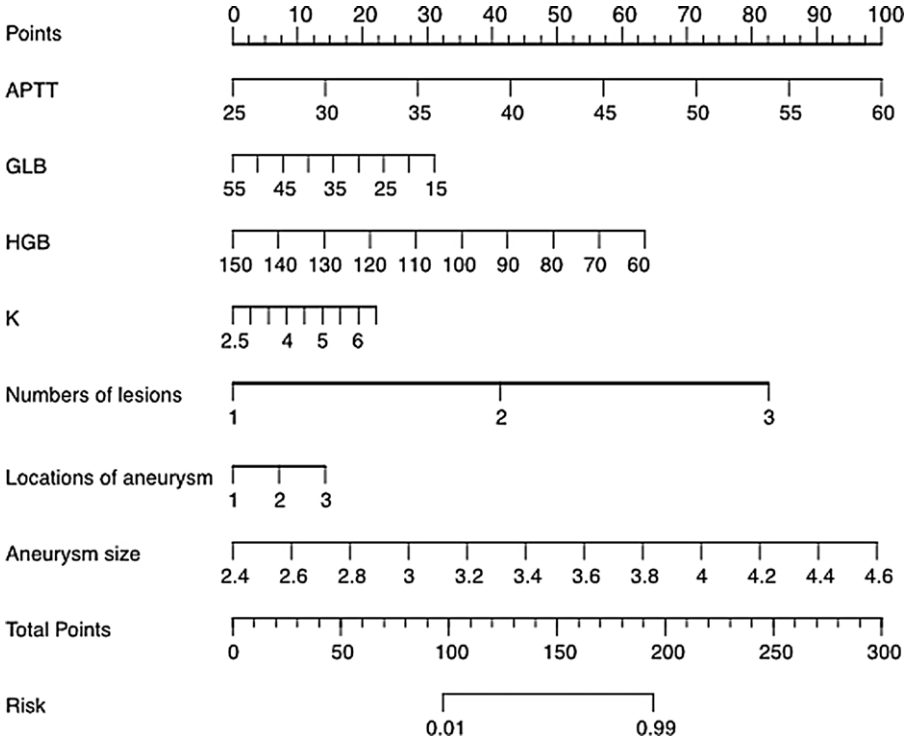

Figure 1. The nomogram prediction scores of univariable analysis.

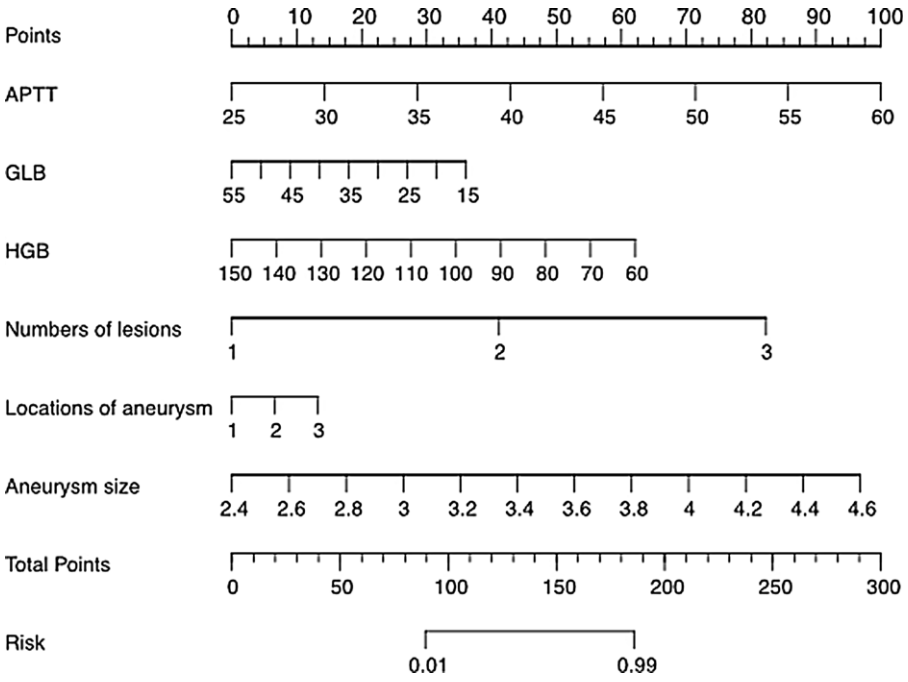

Figure 2. The nomogram prediction scores of multivariable analysis.

yielded a relatively high sensitivity (91.3%) and specificity (92.9%).[32] Consistent with previous findings, our study confirmed that a lower number of lesions, the particular location of the aneurysm, and smaller size of coronary artery aneurysms were the independent factors for predicting coronary artery aneurysms regression, indicating that the severities and sites of aneurysms were significantly associated with the prognosis of coronary artery aneurysms.

For the first time, we confirmed that the level of haemoglobin, globulin, and activated partial thromboplastin time were significantly associated with early coronary artery aneurysms regression. Most importantly, we used nomogram prediction models to involve all identified parameters in this research, which significantly elevated the diagnostic power in distinguishing early coronary artery aneurysms regression. It considered that the laboratory parameters might reflect the biological injuries of endothelial or smooth muscle cells during the Kawasaki disease acute phase. Therefore, the nomogram prediction system involved morphological and biological indicators in improving the diagnostic value.

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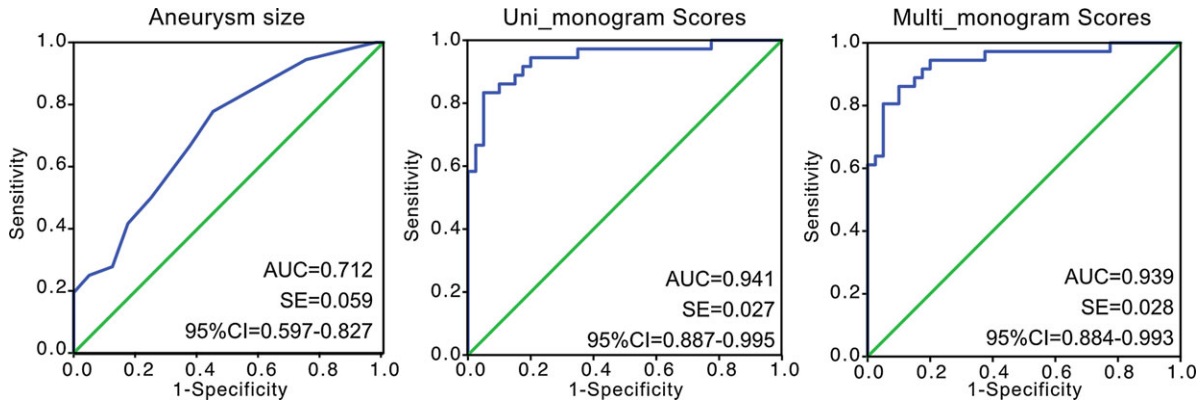

Figure 3. The receiver operating characteristic curves of coronary artery aneurysms size, Uni_nomogram scores, and Multi_nomogram scores.

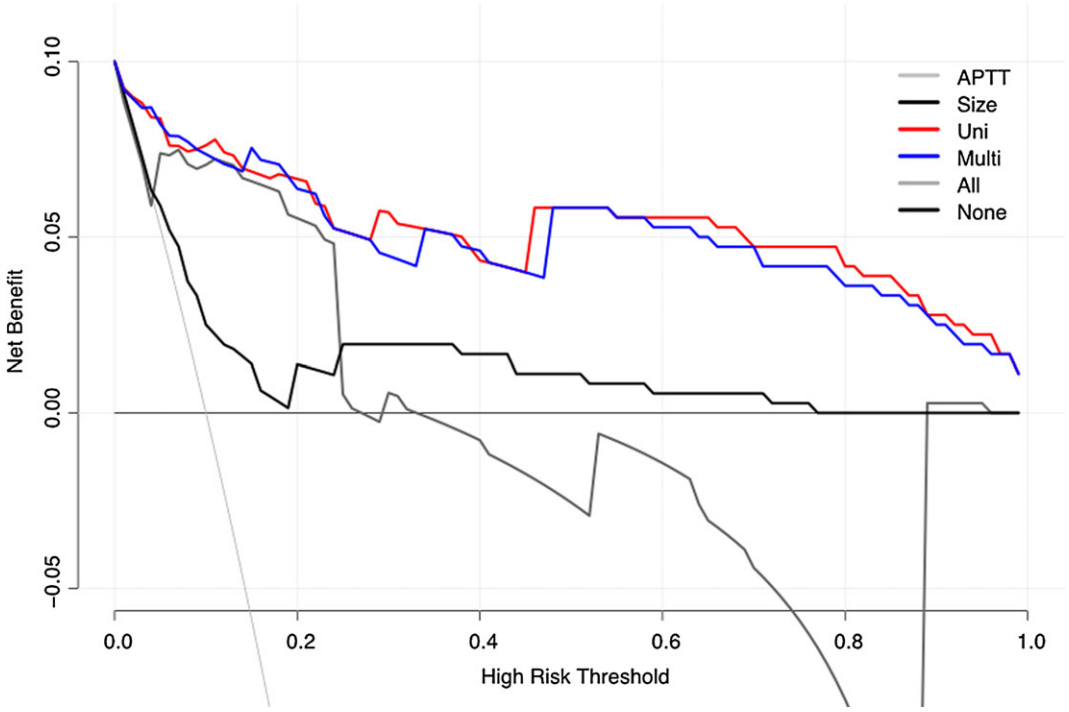

Figure 4. Decision curve analysis based on coronary artery aneurysms size, Uni_nomogram scores, and Multi_nomogram scores at 10% coronary artery aneurysms incidence.

Our study had potential limitations. First, selective bias might have occurred as this study was performed in a single institution. Second, this study was limited by its retrospective design, and the findings should be validated in the prospective cohort in the future.

Conclusion

Our study was the first to demonstrate laboratory parameters associated with coronary artery aneurysms regression, which combined the size of coronary artery aneurysms, the number of lesions, and the location of aneurysms yielded better predictive value for predicting coronary artery aneurysms regression. Additionally, the nomogram prediction system demonstrated great potential in determining early regression of coronary artery aneurysms associated with Kawasaki disease. Both nomogram scores based on univariable and multivariable analyses presented high sensitivity and specificity.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1047951123001610

Data availability statement. All the data had been presented in the manuscript. Other data sets used in this study are available from the corresponding author upon reasonable request.

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Author contribution. He Y, Shao S, and Qiao Y contributed equally to this work. He Y, Shao S, Zhang N, Wang C, Hua Y, Zhou K, and Liu X collected the clinical data. Qiao Y, He Y, and Shao S reviewed the literature and contributed to manuscript drafting; Li Y and Zhang N performed the Nomogram analysis. Wang C and Li Y conceptualised and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Wang C, Liu X, and Li Y were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Competing interests. None.

Ethical standard. This study was approved by the Ethics Committee of West China Second Hospital of Sichuan University (2014-034). And informed consent from all the patient's parents had been obtained, including the patient's clinical and imaging details in the manuscript for the purpose of publication.

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