Efficacy of Four Scoring Systems in Predicting Intravenous Immunoglobulin Resistance in Children with Kawasaki Disease in a Children's Hospital in Beijing, North China

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Objective To evaluate the predictive efficacies of 4 existing scoring systems for intravenous immunoglobulin (IVIG) resistance in Kawasaki disease (KD) in hospitalized children with KD in a children's hospital affiliated with the Capital Institute of Pediatrics, Beijing, China.

Study design We retrospectively analyzed 1569 children with KD treated at our children's hospital between January 2010 and December 2015. Age, sex, clinical manifestations, and pretreatment hematologic indicators were recorded. Scores were assigned using 4 existing scoring systems: Egami, Kobayashi, San Diego, and Formosa. A 4-case table test was used to determine prediction efficacies.

Results There were 63 IVIG-resistant cases (41 males, 22 females; average age, 2.5 years). Nine cases were classified as high risk for IVIG resistance by the Egami system, and this system had a sensitivity of 14% and a specificity of 86%. Ten cases had Kobayashi high-risk scores, and this system had a sensitivity of 16% and a specificity of 85%. The San Diego system assigned 60 cases as high-risk, and had a sensitivity of 95% and specificity of 3%. Finally, 27 cases had Formosa scores in the high-risk category, and this system had a sensitivity of 43% and a specificity of 47%.

Conclusions None of the evaluated systems for assessing the risk for IVIG resistance displayed the combination of sensitivity and specificity necessary for screening. Our analyses show that the 4 scoring systems have limited utility in predicting IVIG resistance among patients with KD in our population. *(J Pediatr 2017;184:120-4).*

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Kawasaki disease (KD) is associated with nonspecific vascular inflammation of primarily medium- and small-sized arteries (particularly the coronary arteries) and is largely seen in children aged <5 years. KD is treated with high-dose intravenous immunoglobulin (IVIG; 2 g/kg/day) in combination with oral aspirin (30-50 mg/kg/day). This treatment can decrease the incidence of coronary artery aneurysms from 20%-25% to 3%-5%.[1] However, 15%-25% of patients with KD still have a fever at 48 hours after the initial IVIG treatment, require a second dose of IVIG or additional treatment,[2] and are at greater risk for coronary aneurysms.[3]

Previous studies have found that IVIG resistance is more common in patients with certain pretreatment laboratory findings: C-reactive protein (CRP) >100 mg/L, lactate dehydrogenase (LDH) >590 IU/L, and hemoglobin <10 g/dL.[4] Sato et al[5] proposed a scoring system based on interleukin (IL)-6 and neutrophil granulocyte percentage (N%) to predict IVIG resistance. Researchers have summarized risk factors in different countries and races to establish the San Diego,[6] Kobayashi,[7] Egami,[8] and Formosa[9] scoring systems for predicting the IVIG treatment response; however, data are lacking on whether these scoring systems are reliable in the Chinese population.

In this study, we aimed to compare the predictive efficacies of the 4 scoring systems for IVIG resistance in patients with KD in the Beijing area. This information is important for medical professionals attempting to individualize therapy to reduce the risk of coronary artery damage in patients with KD.

Methods

In this study, we retrospectively analyzed 1569 children with KD diagnosed and treated at a children's hospital affiliated with the Capital Institute of Pediatrics

CRP	C-reactive protein	LDH	Lactic dehydrogenase
IVIG	Intravenous immunoglobulin	N%	Neutrophilic granulocyte percentage
KD	Kawasaki disease		

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Table I. Scoring systems used to predict IVIG resistance in patients with KD

Scoring systems	Nation	Enrolled patients, n	Patients with IVIG resistance, n	Sensitivity, %	Specificity, %	Risk factors	Points	Predicted risk (score)
Egami	Japan	320	41	78	76	Age <6 mo	1	Low risk (0-2)
						Illness days <4	1	
						CRP ≥8 mg/dL	1	High risk (≥3)
						ALT ≥80 IU/L	2	
						PLT $<300 \times 10^9$/L	1	
Kobayashi	Japan	528	148	86	68	Age <12 mo	1	Low risk (0-3)
						Illness days <4 d	2	
						CRP >10 mg/dL	1	High risk (≥4)
						AST >100 IU/L	2	
						PLT $<300 \times 10^9$/L	1	
						Na ≤133 mmol/L	2	
						N% ≥80%	2	
San Diego	US	362	60	73.3	61.9	Illness <4 d	1	Low risk (0-1)
						GGT ≥60 IU/L	1	
						zHgb ≤–2	1	High risk (≥2).
						% Bands ≥20	2	
Formosa	Taiwan	248	29	86.2	81.3	Positive lymphadenopathy	1	Low risk (0-2)
						N% ≥60%	2	High risk (≥3)
						Albumin <3.5 g/dL	1	

ALB, albumin; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *ESR*, erythrocyte sedimentation rate; *GGT*, gamma-glutamyl transpeptidase; *Hgb*, hemoglobin; *IVIG*, intravenous immunoglobulin; *PLT*, platelet count; *T-Bil*, total bilirubin; *WBC*, white blood cell count.
zHgb = [(observed Hgb) – (mean Hgb for age)]/SD for age.

between January 2010 and December 2015. Inclusion criteria included a definitive diagnosis of KD based on the presence of the following[10]: (1) fever persisting for ≥5 days (except in those cases in which the fever subsided before the fifth day in response to therapy); (2) bilateral conjunctival injection without exudation; (3) changes in the lips and oral cavity (eg, reddening of the lips, rhagades, strawberry tongue, diffuse injection of oropharyngeal mucosa); (4) polymorphous exanthem; (5) changes in the peripheral extremities (eg, reddening of the palms and soles, indurative edema); and (6) acute nonpurulent cervical lymphadenopathy >1.5 cm in diameter, often unilateral. At least 5 of the 6 signs should be satisfied for diagnosis; however, patients meeting 4 criteria can be diagnosed with KD if coronary aneurysm or dilatation is seen on 2-dimensional echocardiography or coronary angiography. All of the children with KD in this study were treated with IVIG (2 g/kg/day) in combination with oral aspirin (30-50 mg/kg/day) after hospital admission.

IVIG resistance was defined as: (1) fever persisting for 48 hours after the IVIG treatment (temperature >38°C); and (2) recrudescent fever within 7 days of IVIG treatment accompanied by the other clinical manifestations of KD.[11] Criteria for exclusion from the study were: (1) recurrent cases; (2) receipt of initial treatment before hospitalization; (3) presence of other vascular inflammatory diseases; and (4) incomplete clinical data for the scoring systems.

All procedures regarding this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Declaration of Helsinki, as revised in 2008. The study was approved by the Ethics Committee of the Capital Institute of Pediatrics (no. 2015040). Informed consent was obtained from a parent or guardian of each patient before the experiment.

Data recorded for all patients included age, sex, clinical manifestations, and pretreatment laboratory indicators: white blood cell count, N%, hemoglobin, platelet count, alanine aminotransferase, aspartate aminotransferase, total bilirubin, gamma-glutamyl transpeptidase, albumin, serum sodium, LDH, CRP, and erythrocyte sedimentation rate. The information used to determine the Egami, Kobayashi, San Diego, and Formosa scores is shown in **Table I**.

The children were assigned scores according to the rules of each scoring system. Four case table test data were acquired based on the scores, and the sensitivity and specificity of each system was used to determine prediction efficacy.

Statistical Analyses

SPSS version 20.0 (IBM, Armonk, New York) was used for statistical calculations. Measurement data are expressed as mean ± SD for normally distributed data or median (IQR) for non-normally distributed data. The 2 independent samples *t* test was used to compare groups of normally distributed data, and the Mann–Whitney *U* test was used to compare groups of non-normally distributed data. The χ^2 test was applied for categorical data. The 4 case table test was used to evaluate the effectiveness of the 4 scoring systems in predicting IVIG resistance. A *P* value <.05 was considered statistically significant.

Results

There were 147 patients with IVIG resistance (9%) among the 1549 children with KD in the present study. Eighty-four patients were excluded from our analysis because the initial IVIG treatment was provided before hospitalization, 61 were excluded because there was no IVIG treatment, and 261 were excluded because the data were incomplete. Finally, 1163 children