Assessment of Risk Scores for Predicting Coronary Artery Abnormalities at a North American Center

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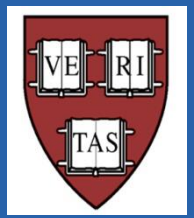

Presenter Disclosure Information

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The authors have no relevant financial relationships.

Purpose

- To assess the performance of established risk scores in identifying KD patients at high risk for developing coronary artery abnormalities (CAA)

- To determine the utility of adding baseline z scores to risk scores

Background

- Currently available standard of care for KD includes high-dose IV Immunoglobulin
- Patients with evolving CAA receive additional treatments (e.g., IVIG retreatment, adjunctive Rx)
- Ability to accurately predict which patients are at high risk for CAA would be helpful in selecting patients for more intense primary therapy.

Background

- Effective risk scores have been developed in Japan to predict IVIG resistance
  - Applicability to North American populations uncertain
  - Sleeper et al 2011
    - Japanese risk scores have low sensitivity for predicting IVIG resistance
- Baseline echocardiogram results are not included in currently available risk scores.
  - Could improve their predictive validity for North American children.

Kobayashi Cut off Point: ≥4	Egami Cut off Point: ≥3	Sano Cut off Point: ≥2	Harada Cut off Point: ≥4
Fever ≤ 4 d	Fever ≤ 4 d		
Age ≤12 mo	Age ≤ 6 mo		Age ≤ 12 mo
			Male
CRP ≥10 mg/dL	CRP ≥8 mg/dL	CRP ≥7 mg/dL	CRP >3 mg/dL
Platelets ≤ 300	Platelets ≤300		Platelets <350 ml
AST ≥ 100	ALT ≥ 80	AST ≥ 200	
Na ≤ 133		Total bilirubin ≥ 0.9 mg/dL	WBC > 12 ml
Neutrophils≥80%]			Hematocrit < 35
			Albumin < 3.5 g/dL

Subjects

- Inclusion Criteria
  - Diagnosis of KD from 1/2006-5/2014
  - Single institution (BCH)
  - Lab data within first 10 days AND ≤1 day prior to IVIG
  - Treatment with IVIG
- Exclusion Criteria
  - Baseline echo data not available
    - must be pre-IVIG or within 48 hours of IVIG
  - No follow up echo in 4-8 weeks after fever onset

Methods

- Retrospective study design approved by IRB
- Data Obtained:
  - Patient factors (e.g., age, sex, race)
  - Medical factors (e.g., day of illness, criteria)
  - Laboratory data (lab components of risk scores)
  - Echo data: coronary artery z scores
- CAA defined as z score ≥2.5 in the RCA or LAD at 4-8 weeks of illness

Analysis

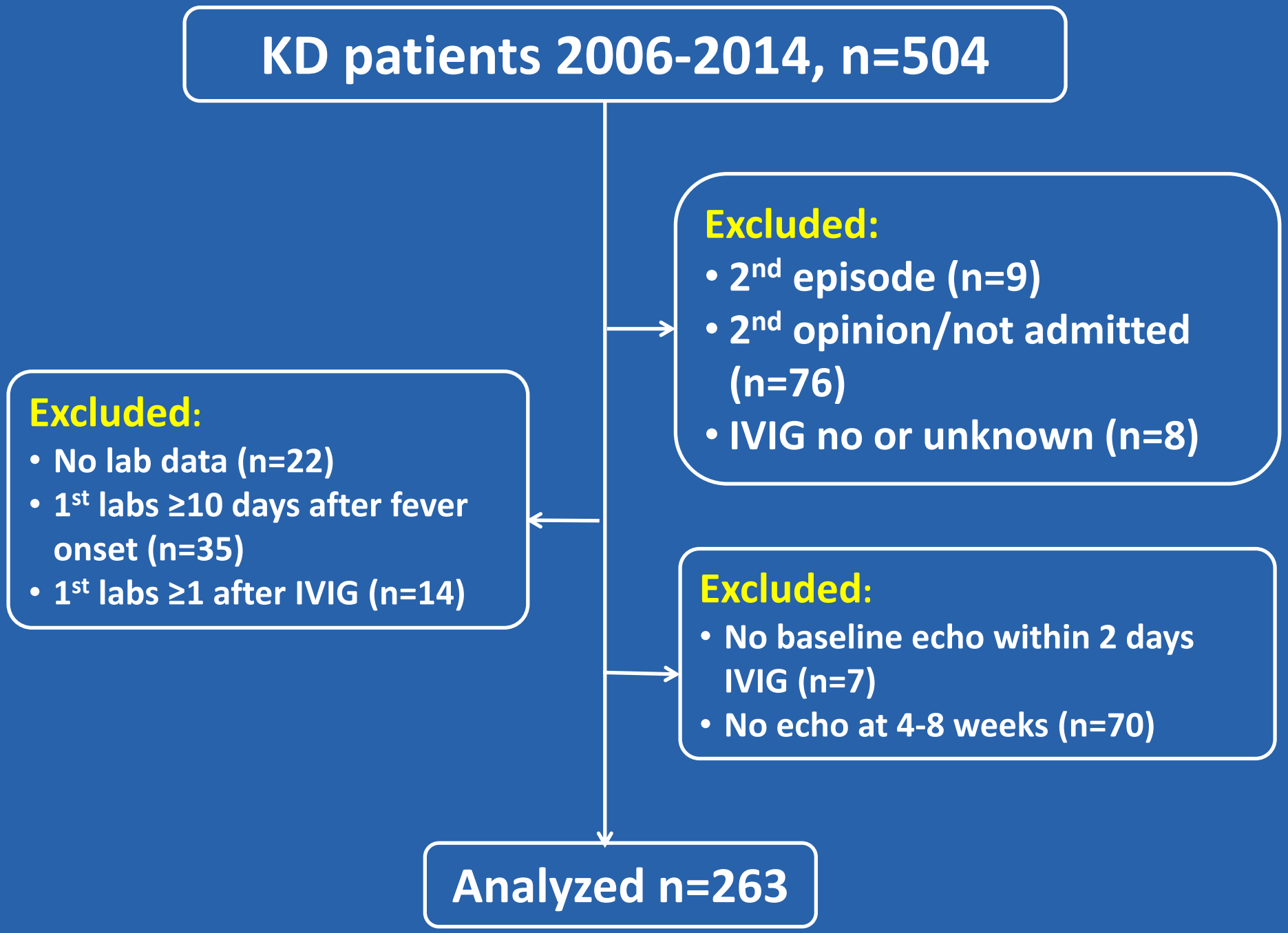
- For each risk score, proportions of patients with CAA were compared for high versus low risk groups using Fisher's exact test
- Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each risk score and for baseline maximum z score (z Max) ≥ 2

Analysis

- The ability of z Max ≥ 2 to improve prediction of CAA beyond risk scores alone was assessed using bivariate logistic regression models
- Logistic regression was also used to evaluate the associations of additional patient demographic and clinical factors with CAA
- Discrimination for each model was quantified using the C statistic

C Statistic

- Equivalent to the area under the receiver-operator characteristic curve (AUC)
- Quantifies how well the model is able to distinguish between patients who develop CAA and those who do not
  - 0.5 indicates a model with no predictive power
  - 1.0 means the model predicts the outcome perfectly
  - 0.7 or higher is considered to represent reasonable discrimination


KD patients 2006-2014, n=504
Excluded:
• 2nd episode (n=9)
• 2nd opinion/not admitted (n=76)
• IVIG no or unknown (n=8)
Excluded:
• No lab data (n=22)
• 1st labs ≥10 days after fever onset (n=35)
• 1st labs ≥1 after IVIG (n=14)
Excluded:
• No baseline echo within 2 days IVIG (n=7)
• No echo at 4-8 weeks (n=70)
Analyzed n=263

Patient Characteristics (n=263)

Variable	N, % or median (range)
Age at Fever Onset	3.1 y (0.1-14.1)
Male Sex n (%)	170 (65%)
Race • White • Black • Asian • Other, including > 1 race • Not Reported	 151 (58%) 25 (10%) 42 (16%) 17 (6%) 28 (10%)
Hispanic	33 (13%)
Days of Fever	7 (2-11)
Clinical Criteria • ≤3 • 4 • 5	 70 (27%) 129 (49%) 64 (24%)
Retreatment with IVIG	69 (26%)

Baseline ECHO Data (n=263)

Z score	Median, range
RCA	0.86 (-2.17, 9.66)
LAD	0.86 (-2.07, 12.1)
Z max	1.50 (-1.35, 12.1)

ECHO Data: Baseline

	Z-score ≥ 2.00	Z-score ≥ 2.50
RCA	47 (19%)	31 (12%)
LAD	57 (23%)	37 (15%)
Z Max	75 (29%)	53 (21%)

ECHO Data: 4-8 Weeks After Fever Onset

CAA (Z score ≥2.5)	15 (6%)

Risk scores and CAA at 4-8 Weeks

	n	# (%) with CAA	P-value
Kobayashi • Low Risk (0-3) • High Risk (≥4)	 147 72	 11 (7%) 2 (3%)	0.23
Egami • Low Risk (0-2) • High Risk (≥3)	 187 51	 12 (6%) 2 (4%)	0.74
Sano • Low Risk (0-1) • High Risk (≥2)	 184 31	 10 (5%) 3 (10%)	0.41
Harada • Low Risk (0-3) • High Risk (≥4)	 77 139	 0 (0%) 12 (9%)	0.005
Baseline Echo Max Z score • <2 • ≥2	 182 75	 3 (2%) 12 (16%)	<0.001

Risk Scores and Baseline Z Scores

	C-statistic	C-statistic (Bivariate)
Kobayashi High Risk Baseline Z max ≥2	0.59	0.84
Egami High Risk Score Baseline Z max ≥2	0.54	0.79
Sano High Risk Score Baseline Z max ≥2	0.55	0.76
Harada High Risk Score	Cannot estimate – No Aneurysms in Low Risk Group	
Baseline Z max ≥2	0.77	

Test Characteristics

	Sensitivity (CAA=15)	Specificity (No CAA=248)	PPV	NPV
Kobayashi High Risk Score	**15%**	**66%**	**3%**	**93%**
Egami High Risk Score	**14%**	**78%**	**4%**	**94%**
Sano High Risk Score	**23%**	**86%**	**10%**	**95%**
Harada High Risk Score	**100%**	**38%**	**9%**	**100%**

Test Characteristics

	Sensitivity (CAA=15)	Specificity (No CAA=248)	PPV	NPV
Baseline Z Max ≥2.00	80%	74%	16%	98%

Multivariable Analyses

	Odds Ratio (95% CI)	P-value	C-statistic
Max Z score at Baseline Echo ≥2.0	11.5 (3.08, 42.9)	<0.001	0.82
Race Asian (includes >1 race reported)	4.38 (1.40, 13.7)	0.01	

Limitations

- Retrospective Chart Review
  - Missing data limited total number of subjects and therefore power
- Very small number of patients with CAA limits the ability to perform multivariable analysis

Conclusions

- Among established Japanese risk scores, only the Harada score predicted the development of CAA at a cosmopolitan North American center.
- Baseline z score ≥2.0 alone was more predictive of CAA than any published risk score alone, and increased the discrimination of all risk scores when added in a bivariate analysis.
- Baseline z score had reasonable sensitivity, and excellent negative predictive value

Inferences

- Baseline z scores may provide the best biomarker for selection of high-risk North American populations for therapeutic trials of adjunctive therapies.
- Future prospective studies should determine
  - Predictive validity of baseline z score for CAA
  - Optimal z score cut-off


EXIT