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ORIGINAL ARTICLE

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Predictors of inadequate initial echocardiography in suspected Kawasaki disease: Criteria for sedation

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Abstract

Objective: Kawasaki disease is the primary cause of acquired pediatric heart disease in developed nations. Timely diagnosis of Kawasaki disease incorporates transthoracic echocardiography for visualization of the coronary arteries. Sedation improves this visualization, but not without risks and resource utilization. To identify potential sedation criteria for suspected Kawasaki disease, we analyzed factors associated with diagnostically inadequate initial transthoracic echocardiography performed without sedation.

Design: This retrospective review of patients < 18 years old undergoing initial transthoracic echocardiography for the inpatient evaluation of suspected Kawasaki disease from 2009 to 2015 occurred at a medium-sized urban children's hospital. The primary outcome was diagnostically inadequate transthoracic echocardiography without sedation due to poor visualization of the coronary arteries, determined by review of clinical records. The associations of the primary outcome with demographics, Kawasaki disease type, laboratory data, fever, and antipyretic or intravenous immunoglobulin treatment prior to transthoracic echocardiography were analyzed.

Results: In total, 112 patients (44% female, median age 2.1 years, median BSA 0.54 m^2) underwent initial transthoracic echocardiography for suspected Kawasaki disease, and 99 were not sedated. Transthoracic echocardiography was diagnostically inadequate in 19 out of these 99 patients (19.2%) and was associated with age ≤ 2.0 years, weight ≤ 10.0 kg, and antipyretic use ≤ 6 hours before transthoracic echocardiography (all $P < .05$). These variables did not reach statistical significance on multivariable analysis.

Conclusions: Patients ≤ 2.0 years or ≤ 10.0 kg or those recently receiving antipyretics, potentially a surrogate for irritability, were associated with diagnostically inadequate transthoracic echocardiography during the inpatient workup of Kawasaki disease. These factors should be considered when deciding which patients to sedate for initial Kawasaki disease transthoracic echocardiography.

KEYWORDS
criteria, fever, Kawasaki disease, pediatric, sedation, transthoracic echocardiography

1 | INTRODUCTION

Kawasaki disease (KD) is an acute multisystem vasculitis of uncertain etiology characterized by a persistent febrile illness in young children that can lead to coronary artery aneurysms, which can be identified

Abbreviations: AHA, American Heart Association; ASA, aspirin; BSA, body surface area; CAs, coronary arteries; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; IVIG, intravenous immunoglobulin; KD, Kawasaki disease; OR, odds ratio; TTE, transthoracic echocardiography; WBCs, white blood cells.

using transthoracic echocardiography (TTE).[1,2] KD has become the primary cause of acquired pediatric heart disease in developed countries.[3] Atypical and incomplete forms of the illness present diagnostic challenges, and strategies to ensure appropriate recognition of all presentations of KD incorporate the use of nonclassical criteria including inflammatory laboratory values, marked irritability or lethargy, and TTE.[1,4] Coronary involvement significantly increases the morbidity and mortality of the disease.[1,5,6] Early intervention with intravenous immune globulin (IVIG) has been shown to reduce the development of coronary artery aneurysms from as high as 25% down to 5%.[7–10] For these reasons, TTE has become a critical component of the diagnosis and management of KD.

In KD, TTE is sometimes performed using sedation due to the irritability and young age of patients and the small structures being examined, particularly the coronary arteries. The use of sedative drugs has come under scrutiny due to emerging evidence of association with developmental neurotoxicity, as well as the increased resources necessary to administer sedation and the small but not negligible risk of acute adverse events.[11–17] These drugs are used variably during KD TTE, with institutional rates ranging from 6% to 100%.[18,19] The KD literature regarding benefits of sedation in pediatric TTE is sparse, but has found better visualization of the coronary arteries.[18] It is recommended by AHA guidelines, however, that TTE not be delayed, even for sedation, once KD is suspected.[1] For these reasons, universal use of sedation is not often employed. However, criteria for which patients would most likely benefit from the use of sedation are not defined. To help elucidate such criteria, this study sought to identify patient or disease characteristics associated with a diagnostically inadequate initial TTE without sedation in patients undergoing inpatient workup for KD.

2 | METHODS

A retrospective review was performed of all patients aged 0 to 18 years undergoing an initial inpatient TTE for evaluation of confirmed or potential KD at the Children's Hospital at Montefiore, an inner-city medium-sized tertiary care facility, from January 2009 until May 2015. The 2009 starting point was chosen as this was when the institution's echocardiography lab reading software was updated and reporting for KD TTEs was standardized to include assessment of 7 coronary artery segments. Patients with greater than low complexity congenital heart disease (simple, isolated lesions such as atrial or ventricular septal defect, bicuspid aortic valve or patent ductus arteriosus), were excluded. The Institutional Review Board of the Albert Einstein College of Medicine and the Research Oversight Committee of the Department of Pediatrics approved this investigation with a waiver of informed consent.

The primary outcome for this study was a "diagnostically inadequate" initial TTE without sedation. "Diagnostically inadequate" was defined as a TTE that was considered insufficient for ruling out coronary artery abnormalities by the treating cardiologist and was repeated within 6 days to complete the echocardiographic evaluation to inform clinical decision making. The primary outcome serves as a surrogate for patients that might have benefited from being sedated on their initial TTE. The study population was purposefully comprised of patients who were not sedated for their initial TTE during workup of KD to better evaluate the patient- and disease-driven characteristics associated with a diagnostically inadequate TTE. Investigator review of TTE reports and clinician notes were used to determine whether an initial TTE was considered diagnostically inadequate by the treating cardiologist. Patients with repeat TTEs performed due to a change in clinical status (not due to poor visualization of CAs) or performed beyond 6 days from the initial were not considered to have diagnostically inadequate studies. Beyond 6 days, the risk that additional echocardiograms were simply routine KD follow up studies is more likely, as our institution typically perform such examinations after about 2 weeks, and these were therefore excluded from the primary outcome. Data from patients who underwent sedation on their initial TTE was excluded from the study's primary analysis, but was included alongside our descriptive statistics to better characterize our KD population. During this time period, the majority of sedations were performed with oral chloral hydrate with an initial dose of 50–70 mg/kg and repeat dosing as needed to a maximum of 1 g for infants $<$ 1 year and 2 g for older children. Starting January 2015, oral pentobarbital was used with an initial dose of 4 mg/kg and repeat dosing (2–4 mg/kg) as needed every 20 minutes to a maximum of 8 mg/kg.

Predictor variables collected included the following: patient weight, age, KD criteria fulfilled, IVIG administration prior to TTE, recent antipyretic (ibuprofen, acetaminophen, aspirin [ASA]) use within 6 hours prior to initial TTE, fever within 1 hour of TTE, number of days since start of KD fever, and inflammatory laboratory markers. The age and weight variables were converted into binary variables ($\leq$ or $>$ 2.0 years and $\leq$ or $>$ 10 kg) as has been done in similar literature[20,21] and for ease-of-use in any resulting management criteria. KD type by criteria fulfilled (Complete, Incomplete) were assigned in accordance with the American Heart Association (AHA)-endorsed KD diagnostic guidelines at the time of the initial KD TTE.[1] A third category of "Suspected KD" was created for the remainder of the patients with a TTE done as part of an initial KD workup who did not meet the diagnostic criteria for Complete or Incomplete KD at that time. Suspected KD was defined as a patient with 5 days of fever with none or 1 clinical criterion and elevated inflammatory laboratory markers. This last category, although not present in clinical guidelines, serves as a working label for those patients who receive a TTE and workup, but who may or may not eventually be diagnosed and treated as KD. This label was hypothesized to provide useful information at the decision-making time point of the initial TTE, but prior to a formal diagnosis.

The laboratory criteria collected for the analysis included those typically associated with KD: erythrocyte sedimentation rate (ESR), C reactive protein (CRP), hemoglobin, hematocrit, platelets, serum white blood cells (WBCs), albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and urine WBCs. All laboratory values used were available to the treating clinician prior to the initial TTE. Coronary arteries (CAs) were divided into 7 segments: left main, left circumflex, proximal and distal left anterior descending, proximal right, distal right and posterior descending arteries. Visualization of each of the 7 coronary artery segments was determined when a measurement of a segment was documented in the TTE report available through the electronic medical record. Diagnostic errors; defined as a diagnosis

meeting AHA criteria that is unintentionally delayed, wrong, or missed (as judged from eventual appreciation of the existing data or more definitive future information);[20] were identified for all subjects by review of subsequent TTE reports.

3 | STATISTICAL ANALYSIS

Descriptive analysis included a summary of patient demographic and clinical characteristics. Their bivariate associations with an initial TTE with sedation versus without, and for diagnostically inadequate TTE versus not were evaluated by the chi-square or Fisher's exact tests for categorical variables and two-sample *t* tests or Wilcoxon rank-sum tests for continuous variables.

Multivariable logistic regression analysis was conducted to identify independent factors associated with diagnostically inadequate initial TTE without sedation. Exact logistic regression was used given that some variables had categories with limited sample sizes. A backward-stepwise approach with likelihood ratio tests was performed for variable selection from the full model with all potential predictors in a multivariable analysis. The variables whose bivariate associations with the outcome had *P* values $< .20$ or which were considered clinically relevant to the outcome were included in the full model. A *P* value $< .05$ was considered statistically significant. Data were analyzed by using SAS software (version 9.4; SAS Institute, Inc, Cary, North Carolina).

4 | RESULTS

Overall, 112 patients underwent initial TTE for KD evaluation over the study period (44% female, median age 2.1 years with interquartile range [IQR] 1.4–2.8 years, median BSA 0.54 m^2 with IQR 0.47–0.68 m^2, Table 1). Of those patients, 99 (88%) were not sedated initially, and comprised the cohort included in the primary outcome analysis (Figure 1). None of the 13 patients sedated for their initial TTE had a diagnostically inadequate examination and were excluded from the primary analysis. Comparing the 13 initially sedated patients with the 99 who were not sedated, there were no statistically significant clinical or demographic differences found, including in the number of CAs visualized (Table 1). One diagnostic error, which was of minor severity (a missed patent foramen ovale), was later noted after an initial TTE without sedation, and no errors were noted for TTEs initially performed with sedation.

Of the 99 nonsedated patients, 19 (19%) had an inadequate TTE. Unplanned, early repeat TTE for these diagnostically inadequate initial TTEs were performed at a median of 2 days after the initial (range 1–6 days). In the inadequate studies, a median of 4.0 coronary artery segments were visualized versus 6.0 segments in those that were adequate ($P < .001$, Table 3). Bivariate comparisons of demographics and disease characteristics between those with inadequate initial TTEs and those with adequate studies are provided in Tables 2 and 3. In the group with inadequate TTE, there were significantly more patients who were younger (63% vs 36% $\leq$ 2.0 years), smaller (37% vs 15% $\leq$ 10.0 kg,), or had use of any antipyretic (84% vs 59%) or only non-ASA antipyretics (79% vs 48%) within 6 hours prior to the initial TTE (all $P < .05$) on bivariate analysis. KD type, day of fever, prior IVIG, fever within 1 hour of TTE, and the KD laboratory markers were not statistically different between patients with adequate and inadequate TTE. When the 19 diagnostically inadequate examinations were repeated, the visualization of CAs improved significantly (median 4 vs 6, $P = .017$). For the repeat examinations, 10 were sedated and 9 were not sedated with no statistical difference in visualization between the groups.

TABLE 1 Description of populations comparing initially sedated vs not initially sedated patients

Variable	Overall KD population (N = 112)	Initially sedated (N = 13)	Not initially sedated (N = 99)	*P* value[a]
Sex				
Male	63 (56%)	7 (54%)	56 (57%)	.85
Female	49 (44%)	6 (46%)	43 (43%)	
Age				
$\leq$ 2.0 y	49 (44%)	8 (62%)	41 (41%)	.17
$>$ 2.0	63 (56%)	5 (38%)	58 (59%)	
Weight				
$\leq$ 10.0 kg	24 (21%)	5 (38%)	19 (19%)	.15[b]
$>$ 10.0 kg	88 (79%)	8 (62%)	80 (81%)	
BSA				
Median (IQR)	0.54 (0.47–0.68)	0.51 (0.44–0.57)	0.54 (0.48–0.72)	.15[c]
KD Type				
Complete	53 (47%)	6 (47%)	47 (48%)	.90
Incomplete	46 (41%)	5 (38%)	41 (41%)	
Suspected	13 (12%)	2 (15%)	11 (11%)	
Diagnostically inadequate TTE	19 (17%)	0 (0%)	19 (19%)	.12[b]
Visualized CAs				
median (range)	6 (1–7)	6 (2–7)	6 (1–7)	.56[c]

[a]*P* values are calculated using chi-square for categorical variables and the *t* test for continuous variables except as indicated.
[b]*P* value calculated using Fisher's exact test.
[c]*P* value calculated using Wilcoxon rank-sum test.

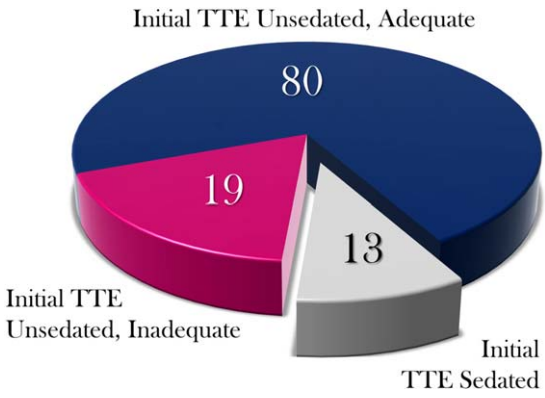

FIGURE 1 Kawasaki disease overall population breakdown

TABLE 2 Comparisons of categorical variables between diagnostically adequate vs inadequate TTE

Population (N)	Diagnostic TTE (80)	Inadequate TTE (19)	*P* value[a]
Sex			
Male	44 (55%)	12 (63%)	.52
Female	36 (45%)	7 (37%)	
Age			
≤ 2.0 y	29 (36%)	12 (63%)	.032[b]
> 2.0	51 (64%)	7 (37%)	
Weight			
≤ 10.0 kg	12 (15%)	7 (37%)	.048[b,c]
> 10.0 kg	68 (85%)	12 (63%)	
KD Type			
Complete	35 (44%)	12 (63%)	.13
Incomplete	37 (46%)	4 (21%)	
Suspected	8 (10%)	3 (16%)	
IVIG treatment before initial TTE	22 (28%)	6 (32%)	.72
Febrile within 1 hour of initial TTE[d]	25 (31%)	6 (33%)	.86
Any antipyretic use ≤ 6 h before initial TTE	47 (59%)	16 (84%)	.038[b]
Non-ASA antipyretic use ≤ 6 h before initial TTE	31 (48%)	11 (79%)	.041[b]

[a]*P* values are calculated using Chi squared for categorical variables except as indicated.
[b]Indicates significance.
[c]Incomplete data, N = 18 for the Inadequate TTE group.
[d]*P* value calculated using Fisher's exact test.

TABLE 3 Comparisons of continuous and ordinal variables between adequate vs inadequate TTE

Predictor variable (N,N′)[a]	Diagnostic TTE	Inadequate TTE	*P* value[b]
Urine WBCs (N = 5312)			
0 to < 5	23 (43%)	4 (33%)	.28[c]
5 to < 11	11 (21%)	3 (25%)	
11 to < 21	10 (19%)	1 (8.3%)	
21 to < 51	6 (11%)	1 (8.3%)	
51 to < 100	3 (6%)	2 (17%)	
≥ 100	0	1 (8.3%)	
ESR (N = 6713)	63.3 (29)	76.5 (40)	.16
CRP (N = 6616)	9.1 (6)	11.3 (11)	.44
Serum WBCs (N = 7919)	14.1 (6.4)	18.0 (11)	.15
Hemoglobin (N = 7919)	10.7 (1.1)	11.0 (1.6)	.48
Hematocrit (N = 7919)	31.6 (3.2)	32.6 (4.4)	.26
Platelets (N = 7919)	331 (147)	414 (255)	.18
Albumin (N = 7918)	3.6 (0.5)	3.7 (0.5)	.46
AST/SGOT (N = 6918)	39 (29–56)	31.5 (27–64)	.73[d]
ALT/SGPT (N = 7918)	24 (16–74)	29 (15–81)	.78[d]

[a]Incomplete data, population size for diagnostic TTE (N) and Inadequate TTE (N′) groups, indicated next to each predictor.
[b]All data are expressed as mean (SD) except as indicated. All *P* values are calculated using the *t* test for continuous variables except as indicated.
[c]Data are expressed as N (%), *P* value calculated using Fisher's exact test.
[d]Data are expressed as Median (IQR), *P* value calculated using Wilcoxon rank-sum test.

Table 4 summarizes the results from the final multivariable model. In the full model, we included age, KD type, antipyretic use, serum WBCs, platelets, and fever within 1 hour of TTE. Among the variables with bivariate associations of $P < .20$, weight was excluded due to its known close interdependence with age and ESR was excluded due to many missing values in the dataset. Fever within 1 hour of TTE which was considered clinically relevant to the primary outcome was additionally included. The final model included younger age (≤ 2.0 years) and antipyretic use < 6 hours from the initial TTE, however, while younger age approached statistical significance ($P = .06$, OR 2.67), it did not reach it.

5 | DISCUSSION

In this study, cohort of 99 patients not sedated for their initial TTE during workup of KD, 19 (19%) had "diagnostically inadequate" examinations requiring unplanned, early repeat TTE. While there were a few factors including age ≤ 2.0 years, weight ≤ 10 kg, and antipyretic use that were significant on bivariate analysis, none of these factors maintained significance on multivariable analysis.

In a prior investigation, KD itself was found to be an independent risk factor for early unplanned repeat TTE.[21] The current investigation further explores this finding by highlighting the specific KD characteristics associated with inadequate TTE. Younger age has been previously reported in the general pediatric echocardiography literature,[21,22] and our bivariate data support this finding. It is intuitive that younger patients who ordinarily have difficulty cooperating with a TTE would also present a challenge during an acute KD illness, where irritability is a hallmark of the disease.[1,23,24] Further, our data suggest a possible association with recent antipyretic use, which is a new finding. It is interesting to note that although antipyretic use was significant on bivariate association analysis, fever concurrent with TTE (within an hour) was not. One explanation for this may be that non-ASA antipyretic use is a surrogate indicator of subjective irritability, as antipyretic

TABLE 4 Results from the final multivariable model[a] for diagnostically inadequate TTE

	P value	Odds ratio	95% CI
Age ≤ 2.0 years	.06	2.76	0.96–7.93
Antipyretic use ≤ 6 h before initial TTE	.10	3.42	0.83–19.54

[a]The backward variable selection for multivariate analysis was performed starting from the full model, which included and eliminated stepwise the following variables: age, any antipyretic use, Kawasaki disease type, platelets, serum white blood cells, fever.

medications are sometimes used in irritable children and not necessarily for fever. Also, the recent administration of antipyretic medications may have resolved fever between administration and TTE performance. It is logical that especially irritable or recently febrile patients would have more difficulty tolerating an echocardiogram sufficiently to obtain diagnostic images. However, we cannot prove that patients who had been given antipyretics were more irritable. Our medical records did not allow us to determine irritability level as the routine documentation of pain scales was incomplete.

Our data show that the majority of initial KD TTEs performed without sedation (81%) were sufficient for diagnostic purposes. Even after an initial inadequate attempt, 9 of 19 repeat studies were adequate when performed again without sedation. Of these 19 patients, the other 10 were sedated for their repeat examinations. Because the entire population undergoing TTE for workup of KD included 112 patients, and 13 were initially sedated, the population was sedated at an overall rate of 23 out of 112 (21%) to obtain adequate diagnostic information. This raises questions. What is an acceptable rate of diagnostically inadequate TTE in KD? What is a reasonable percentage of children that would be expected to require sedation? To answer this question, one must consider the risks and benefits of sedation. Such acute risks include apnea, hypotension, bradycardia, somnolence, and rare allergic reaction.[25,26] The FDA recently warned of evidence that repeated use of sedative/anesthetic drugs in children younger than three years causes neurotoxicity and developmental effects.[12] This series indicates the universal use of sedation for initial KD TTE is not necessarily warranted. However, preemptive use of sedation in patients less than 2 years of age and in particularly irritable or recently febrile patients may reduce the rate of repeat examinations and the related resource utilization. No other disease characteristic evaluated (KD criteria, day of fever, or laboratory values) was useful in predicting who would have a diagnostically inadequate TTE. Current criteria for TTE sedation are lacking and individual practice and interpretation of risk-benefit ratios will vary. We therefore present this data to better inform the treating physician when making the important decision to sedate a young child for initial KD TTE.

At our institution, there are no formal criteria for sedation of KD patients, and the decision is physician-dependent. Patients initially sedated for their TTE were excluded from the primary analysis, as the analysis was intended to identify patient and disease characteristics associated with a diagnostically inadequate TTE. If sedated patients, of whom none had diagnostically inadequate TTE, were included, their characteristics would then not be properly associated with the primary outcome. For example, a physician may have chosen to sedate a child because they were anticipated to have a diagnostically inadequate examination if sedation was not used. Therefore, instead of being associated with the outcome of a diagnostically inadequate TTE, important patient or disease characteristics would be associated with adequate TTE.

Limitations of this investigation include the subjectivity of the primary outcome, "diagnostically inadequate" initial TTE, as it is sometimes difficult to completely determine the indication for a repeat TTE on retrospective review, particularly if documentation of the clinician's thought process and reasoning is incomplete. However, investigator review of clinical notes and TTE reports was used to review charts in detail to ensure our clinical thresholds for a diagnostically inadequate TTE were met. Additionally, objective data such as the number of coronary artery segments visualized was significantly higher in the non-repeated TTEs, lending further confidence that the initial studies which had to be repeated were diagnostically inadequate. As this was a single-center study, results may not be readily generalizable across all institutions. Our small number of inadequate TTEs also resulted in low power for multivariable analysis.

In summary, younger and smaller patients aged up to 2 years and weighing up to 10 kg, and those recently receiving antipyretics, potentially a surrogate for irritability or recent fever, were more likely to have a diagnostically inadequate TTE for KD in our bivariate associations. However, these variables did not maintain significance on multivariable analysis. Other disease characteristics such as disease type, duration and inflammatory markers were not predictive of inadequate TTE. These data may be useful in deciding which patients to sedate for initial TTE evaluation for KD. Future investigations should attempt to quantify irritability in this population, which may be useful as a predictor for the need for sedation.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Participated in study design, collected the data, carried out the initial analysis, drafted the initial manuscript, and approved the final manuscript as submitted: Dr. Lorenzoni.

Participated in study design and carried out the final statistical analysis for the study: Dr. Choi.

Participated in study design, reviewed and revised the manuscript, and approved the final manuscript as submitted: Drs. Choueiter, Katyal, and Munjal.

Oversaw the design and execution of the study and approved the final manuscript as submitted: Dr. Stern.

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REFERENCES

[1] Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation*. 2004; 110(17):2747–2771.

[2] Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria* for the classification of childhood vasculitides. *Ann Rheum Dis*. 2005;65(7):936–941.

[3] Taubert KA, Rowley AH, Shulman ST. Nationwide survey of Kawasaki disease and acute rheumatic fever. *J Pediatr*. 1991;119(2):279–282.

[4] Harada K. Intravenous γ-globulin treatment in Kawasaki disease. *Acta Paediatr Jpn*. 1991;33(6):805–810.

[5] Kitano N, Suzuki J, Takeuchi T, et al. Epidemiologic features and prognostic factors of coronary artery lesions associated with Kawasaki disease based on a 13-year cohort of consecutive cases identified by complete enumeration surveys in Wakayama, Japan. *J Epidemiol*. 2014;24(5):427–434.

[6] Falcini F, Capannini S, Rigante D. Kawasaki syndrome: an intriguing disease with numerous unsolved dilemmas. *Ped Rheum*. 2011;9:17

[7] Gedalia A. Kawasaki disease: 40 years after the original report. *Curr Rheum Rep*. 2007;9(4):336–341.

[8] Kim TY, Choi WS, Woo CW, et al. Predictive risk factors for coronary artery abnormalities in Kawasaki disease. *Eur J Pediatr*. 2007;166(5):421–425.

[9] Kato H, Sugimura T, Akagi T, et al. Long-term consequences of Kawasaki disease. *Circulation*. 1996;94(6):1379–1385.

[10] Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. *NEJM*. 1986;315(6):341–347.

[11] Rappaport BA, Suresh S, Hertz S, et al. Perspectives: anesthetic neurotoxicity - clinical implications of animal models. *NEJM*. 2015;372(9):796–797.

[12] FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnancy women. FDA Drug Safety Communication. www.fda.gov/Drugs/DrugSafety/ucm532356.htm. 14 Dec 2016. Accessed February 1, 2017.

[13] Soriano SG, Vutskits L. Is There Evidence for Long-Term Neurocognitive Effects of Sedatives? Pediatric Sedation outside of the Operating Room: A Multispecialty International Collaboration. Springer Science, Business Media. New York. 2015: 553–558.

[14] Backeljauw B, Holland SK, Altaye M, Loepke AW. Cognition and brain structure following early childhood surgery with anesthesia. *Pediatrics*. 2015;136(1):e1–12.

[15] Glatz P, Sandin RH, Pedersen NL, et al. Association of anesthesia and surgery during childhood with long-term academic performance. *JAMA Pediatr*. 2017;171(1):e163470

[16] Heistein LC, Ramaciotti C, Scott WA, et al. Chloral hydrate sedation for pediatric echocardiography: Physiologic responses, adverse events, and risk factors. *Pediatrics*. 2006;117(3):e434–e441.

[17] Cravero JP, Blike GT, Beach M, et al. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the pediatric sedation research consortium. *Pediatrics*. 2006;118(3):1087–1096.

[18] Margossian R, Lu M, Minich LLA, et al. Predictors of coronary artery visualization in Kawasaki disease. *J Am Soc Echocardiogr*. 2011;24(1):53–59.

[19] Ronai C, Hamaoka-Okamoto A, Baker AL, et al. Coronary artery aneurysm measurement and Z score variability in Kawasaki disease. *J Am Soc Echocardiogr*. 2016;29(2):150–157.

[20] Stern KWD, Gauvreau K, Geva T, Benavidez OJ. The impact of procedural sedation on diagnostic errors in pediatric echocardiography. *J Am Soc Echocardiogr*. 2014;27(9):949–955.

[21] Stern KWD, Chen C, Cohen HW, et al. Unplanned repeat echocardiography with sedation in children: patient risk factors. *Pediatr Cardiol*. 2016;37(6):1057–1063.

[22] Benavidez OJ, Gauvreau K, Jenkins KJ, Geva T. Diagnostic errors in pediatric echocardiography. *Circulation*. 2008;117(23):2995–3001.

[23] Newburger JW, Takahashi M, Burns JC. Kawasaki disease. *J Am Coll Cardiol*. 2016;67(14):1738–1749.

[24] McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American heart association. *Circulation*. 2017;135(17):e927–e999.

[25] Nordt SP, Rangan C, Hardmaslani M, et al. Pediatric chloral hydrate poisonings and death following outpatient procedural sedation. *J Med Toxicol*. 2014;10(2):219–222.

[26] Chicka MC, Dembo JB, Mathu-Muju KR, et al. Adverse events during pediatric dental anesthesia and sedation: a review of closed malpractice insurance claims. *Pediatr Dent*. 2012;34(3):231–238.

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