Temperature-Adjusted Respiratory Rate for the Prediction of Childhood Pneumonia

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Abstract

Objectives: As both fever and pneumonia can be associated with tachypnea, we investigated the relationship between body temperature and respiratory rate (RR) in young children and whether temperature-adjusted RR enhances the prediction of pneumonia.

Methods: In this retrospective cross-sectional analysis of 91,429 children < 5 years of age presenting to an urban pediatric emergency department, the relationship between triage RR and temperature was analyzed using regression analysis. We assessed the predictive value of temperature-adjusted RR for the diagnosis of pneumonia; diagnostic performance was evaluated for continuous RR as well as World Health Organization (WHO) age-based RR thresholds.

Results: The mean RR increased 2.6 breaths/minute for each 1°C increase in temperature. Interpatient variability was comparatively large; at any temperature, the interquartile range (75th percentile minus 25th percentile) varied from 4 to 16 breaths/minute. For predicting pneumonia, temperature- and age-adjusted RR was superior to age-adjusted RR: area under the curve (AUC) = 0.76 (95% confidence interval [CI], 0.75−0.78) versus AUC = 0.73 (95% CI, 0.72−0.75), respectively. Using WHO RR criteria, temperature-adjusted RR improved diagnostic discrimination, as the AUC increased from 0.58 (95% CI, 0.57−0.59) to 0.72 (95% CI, 0.70−0.73).

Conclusions: The effects of temperature on respiratory rate are modest, with a mean increase of 2.6 breaths/minute for each 1°C rise in temperature. Despite considerable interpatient variability in respiratory rates by temperature, temperature adjustment improves the diagnostic value of respiratory rate for pneumonia.

Keywords: diagnosis; fever; pediatric; pneumonia; respiratory rate; temperature

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What's New

Changes in respiratory rate due to fever are modest and may be difficult to appreciate given baseline variability within age strata. However, temperature-adjusted respiratory rates predict pneumonia better that unadjusted respiratory rates and should be considered in diagnostic strategies.

Pneumonia represents one of the most common infections among children with acute febrile illnesses, even in developed countries with high immunization rates.[1] Discriminating children with uncomplicated upper respiratory infections from those with lower respiratory infections is a basic, yet challenging, scenario for frontline clinicians. To identify children with pneumonia, tachypnea is considered a key, albeit weak, predictor and is the primary determinant used by the World Health Organization (WHO) in low-resource settings.[2−8] However, tachypnea is also known to be a physiologic response to fever.[9,10] In most prior investigations of clinical predictors of pneumonia, the influence of fever on respiratory rate (RR) has not been considered. The relationship between fever and respiratory rate has been previously explored in a limited number of studies,[11−14] including a prospective observational study of 1555 febrile patients under 16 years of age being evaluated for lower respiratory tract infection.[12] Importantly, prior investigations had conflicting results on the importance of fever on respiratory rate.[11,13,15,16]

We focused this investigation on the relationship between body temperature and respiratory rate in children less than 5 years of age to determine if temperature-adjusted respiratory rate is a better predictor of pneumonia than unadjusted respiratory rate. If temperature-adjusted respiratory rate proves to be a better indicator of pneumonia, then clinicians might be better guided in the selective use of both chest radiography and antibiotics.

Patients and Methods

Design, Patients, and Data Source

This was a retrospective database review of emergency department (ED) records at a large, urban, tertiary-care

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pediatric hospital with 60,000 ED visits per year. Children less than 5 years of age presenting between January 1, 2012, and March 31, 2017, with a paired temperature and RR at triage were studied. Patients with RRs of <10 or >100 breaths/minute or with temperatures of <35˚C or >41.5˚C or those with chronic comorbid conditions[17] were excluded. The primary diagnostic codes were drawn from the emergency physicians' electronic record. Prior investigations at the study institution indicate high reliance on chest radiographs for the diagnosis of pneumonia, similar to most EDs in the United States.[18–20] For all analyses, patients with the following respiratory diagnoses that might affect respiratory rate were excluded: asthma, bronchiolitis, bronchospasm, empyema, pleural effusion, pleuritis, pneumonitis, pneumothorax, reactive airway disease, or wheezing (see Supplementary Table 1 for International Classification of Disease codes). Furthermore, patients who received albuterol, levalbuterol, or racemic epinephrine nebulization during the ED visit were also excluded for this analysis as another potential indicator of bronchospasm or stridor if not identified by diagnostic code. Children with pneumonia were included in the analyses for predicting pneumonia but were excluded for initial analyses examining the relationship between respiratory rate and temperature.

Vital sign measures within 15 minutes of each other were considered paired regardless of order. Our general practice is to obtain rectal temperatures in infants less than 6 months of age and temporal artery temperatures for those over 6 months of age. The standard nursing technique for respiratory rate in infants and young children is to count for 30 seconds to calculate the respiratory rate per minute.

ANALYTIC PLAN

AGE-STRATIFIED RELATIONSHIP BETWEEN TEMPERATURE AND RESPIRATORY RATE

Using the subset of patients without a pneumonia diagnosis, the relationship between respiratory rate and temperature was graphically depicted using box-whisker displays within age strata (0 to <12 months, 12 to <24 months, 24 months to 5 years). We calculated 90th and 95th percentile thresholds of respiratory rate by degree of temperature and age stratification, as these thresholds are often used to define tachypnea by age.[12]

We assessed the statistical association between respiratory rate and temperature among patients without a pneumonia diagnosis. To properly characterize this relationship, we designated respiratory rate as the dependent variable and compared the following set of ordinary least-squares regression models: 1) linear model, where temperature was modeled as a continuous independent variable; 2) quadratic model, with temperature (centered at the sample mean) and the square of mean-centered temperature as the independent variables, to test for curvature of the respiratory rate-temperature association; and 3) piecewise linear spline model, where the association between respiratory rate and temperature was divided into 4 linear segments, with boundaries of the segments ("knots") placed at the quartiles of temperature. Model fit was assessed using Akaike information criterion, Bayesian information criterion, and the model r-squared.[21,22] Interaction terms for age groups (0 to <12 months, 12 to <24 months, 24 months to 5 years) were tested in the best-fitting model to determine whether the association between respiratory rate and temperature differed by age.

RELATIONSHIP BETWEEN TEMPERATURE-ADJUSTED AND -UNADJUSTED RESPIRATORY RATES AND THE DIAGNOSIS OF PNEUMONIA

Using the full sample of patients with and without pneumonia, we performed logistic regression analysis with pneumonia as the dependent variable to investigate the predictive ability of respiratory rate (as a continuous value), using the area under the receiver operator characteristic curve (AUC) as the metric of classification performance. We then tested whether the inclusion of temperature and age improved the predictive value of respiratory rate by comparing the AUCs of the models. To explore the practical application of temperature-adjusted respiratory rates, this analysis was repeated using 2 different age-based respiratory rate thresholds: 1) respiratory rate cutpoints established by WHO for the identification of pneumonia (>60 breaths/minute for <2 months of age, >50 breaths/minute for 2 to 12 months of age, and >40 breaths/minute for 1 to 5 years of age);[3,23] and 2) using the 90th and 95th percentile RR threshold (defined within age strata and temperature) as measured in this study population.

The study was approved by the institutional review board as a retrospective database study.

RESULTS

STUDY POPULATION

Data from 138,576 children less than 5 years of age were analyzed. Of these, 45,918 were removed for one or more exclusion criteria (Supplementary Figure), and an additional 1229 were initially removed with a diagnosis of pneumonia, leaving 91,429 patients for the primary analysis relating respiratory rate to temperature in the absence of lower respiratory tract conditions. Fifty-six percent of the sample was male, and the median age was 21.4 months (interquartile range [IQR], 10.1−37.7); 30% of patients were <12 months of age, 25% were 12 to 23 months, and 45% were 24 to 60 months. The median triage temperature was 37.0˚C (IQR, 36.7−37.6). Eighty-two percent (n = 75,414) had a temperature less than 38.0˚C; 11% (n = 10,227), 38.0˚C to 38.9˚C; 5% (n = 4595), 39.0˚C to 39.9˚C; and 1.4% (n =1249), ≥40.0˚C.

RELATIONSHIP BETWEEN TEMPERATURE AND RESPIRATORY RATE

Age-based temperature and respiratory rate 90th and 95th centile thresholds are included in Table 1. The age-group variability in respiratory rate by temperature within

Table 1. 90th and 95th Percentiles of Respiratory Rate, Stratified by Triage Temperature and Age

	Triage Temperature (°C)						
Age and Percentile	36.0–36.4	36.5–37.4	37.5–38.4	38.5–39.4	39.5–40.4	40.5–41.5	Total
<12 mo	(2347)	(16,776)	(5264)	(2,040)	(610)	(84)	(27,121)
90th percentile	46	48	52	54	60	60	50
95th percentile	50	56	56	60	64	68	56
12–23 mo	(2500)	(13,248)	(4026)	(2109)	(888)	(152)	(22,923)
90th percentile	32	36	40	44	48	52	38
95th percentile	36	40	44	48	53	60	42
24–60 mo	(4917)	(25,556)	(6683)	(3032)	(1048)	(149)	(41,385)
90th percentile	28	28	32	36	40	44	32
95th percentile	30	32	36	40	44	50	34
Total	(9764)	(55,580)	(15,973)	(7181)	(2546)	(385)	(91,429)
90th percentile	36	40	44	48	48	52	42
95th percentile	40	48	48	52	56	60	48

Values in parentheses represent the sample size for the given triage temperature/age category combination.

strata of age group is depicted in Figure 1; the IQR (75th percentile minus 25th percentile) for each integer degree of temperature ranged from 12 to 16 breaths/minute for infants less than 12 months of age, 6 to 12 breaths/minute for those 12 to 23 months of age, and 4 to 12 breaths/minute for children 24 to 60 months of age.

A comparison of the 3 regression models is provided in Table 2. Across all 3 fit indices, the piecewise linear spline model achieved the best fit; however, all models found a statistically significant, positive, monotonic association between respiratory rate and temperature, characterized by a minor increase in respiratory rate for each 1°C increase of temperature. For conceptual understanding, the linear model can be considered as a succinct description of the relationship, with a mean increase of 2.6 breaths/minute for each 1°C increase of temperature.

The spline model revealed an S-shaped relationship, with each segment of the line exhibiting a positive association between temperature and respiratory rate but with the magnitude of the association varying by temperature quartile. There was an average 1.91 increase in respiratory rate (per minute) for each 1°C increase in temperature over the first quartile of temperature, followed by average respiratory rate increases of 3.80, 3.72, and 2.00 for each 1°C increase in temperature over the second, third, and fourth quartiles, respectively. Interaction terms between spline variables and the categorical age variable revealed that the linear piecewise association between respiratory rate and temperature also differed significantly by age group (P values $<$ .05). Age group-specific coefficients from separate spline models are provided in Supplementary Table 2. Figure 2 displays the spline model regression lines by age group.

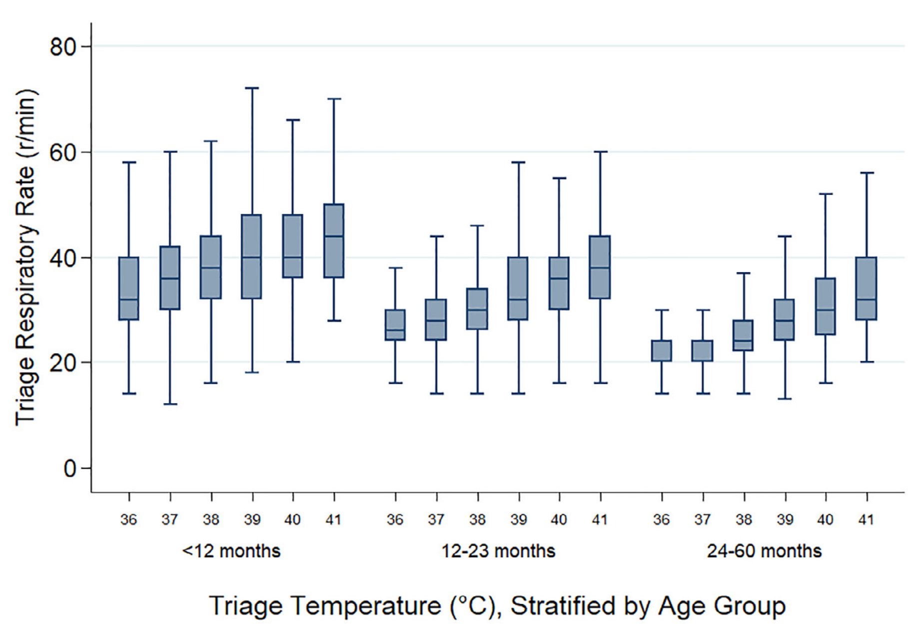

Figure 1. *Relationship of respiratory rate and body temperature, stratified by age group.*

Table 2. Comparison of Modeling Strategies for Assessing the Relationship Between Respiratory Rate and Temperature Among Pediatric Patients Without Pneumonia (N = 91,429)

	Modeling Strategy		
	Linear	Quadratic	Piecewise Linear Spline*
Model Fit Indices			
AIC	7.193	7.192	7.191
BIC	6,072,816	6,066,640	6,062,972
R-squared	0.0619	0.0627	0.0632
Model parameters, mean (95% CI)†			
Temperature	2.61 (2.55, 2.68)	2.91 (2.82, 3.01)‡	N/A
Temperature squared	N/A	−0.24 (−0.30, −0.19)§	N/A
Spline segment 1	N/A	N/A	1.91 (1.40, 2.41)
Spline segment 2	N/A	N/A	3.80 (3.10, 4.50)
Spline segment 3	N/A	N/A	3.72 (3.35, 4.09)
Spline segment 4	N/A	N/A	2.00 (1.86, 2.13)

AIC indicates Akaike information criterion; BIC, Bayesian information criterion; CI, confidence interval; and N/A, not applicable.
*Piecewise linear spline with knots placed at the 25th (36.7°C), 50th (37°C), and 75th (37.6°C) percentiles of temperature.
†Values represent model coefficient (95% confidence interval).
‡Represents the change in respiratory rate for a 1°C increase in temperature from the sample mean.
§The negative coefficient for the quadratic term indicates a concave curvature of the best-fitting line over the range of temperature values.

RELATIONSHIP AMONG RESPIRATORY RATE, TEMPERATURE, AND PNEUMONIA

For the analysis related to pneumonia, the 1229 patients with a pneumonia diagnosis were reintroduced into the dataset, for a total sample of 92,658. The median age and temperature of the pneumonia patients were 26.2 months (IQR, 15.1−39.6) and 37.7°C (IQR, 37.0−38.6), respectively.

The performance of respiratory rate, age-adjusted respiratory rate, and both age- and temperature-adjusted respiratory rate in the prediction of pneumonia is shown in Table 3. Within age strata, the inclusion of temperature with respiratory rate improves the prediction of pneumonia over respiratory rate alone: AUC = 0.76 (95% CI, 0.75−0.78) versus AUC = 0.73 (95% CI, 0.72−0.75). Similarly, temperature can improve the discrimination of pneumonia using the WHO respiratory rate thresholds; the AUC increased from 0.58 (95% CI, 0.57−0.59) to 0.72 (95% CI, 0.70−0.73). Using a 90th or 95th percentile cutpoint for respiratory rate (age and temperature adjusted) poorly discriminated patients with pneumonia AUC values of 0.61 and 0.58, respectively.

DISCUSSION

Using a large cohort of children less than 5 years of age presenting to an urban pediatric ED, we determined that respiratory rate exhibited a small, positive association with temperature that varied in magnitude by temperature quartile and age group. As a heuristic characterization of the relationship, respiratory rate can be said to increase on average 2.6 breaths/minute for

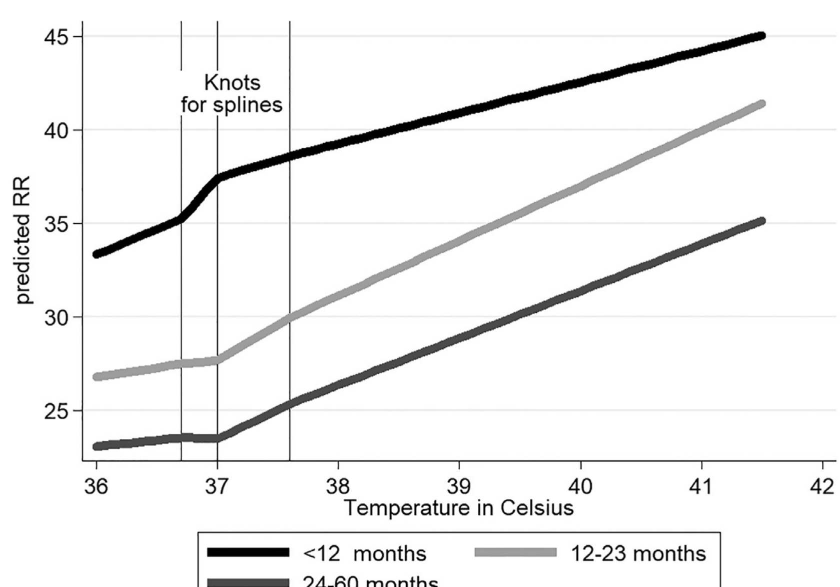

Figure 2. *Spline model regression lines for the relationship of respiratory rate and body temperature, stratified by age group.*

Table 3. Prediction of Pneumonia Using Different Configurations of Respiratory Rate

Predictor(s)	AUC (95% CI)
Respiratory rate	0.67 (0.65−0.68)
Respiratory rate and temperature	0.72 (0.71−0.74)
Respiratory rate and age group	0.73 (0.72−0.75)
Respiratory rate, temperature and age group*	0.76 (0.75−0.78)
WHO respiratory rate cutpoints	0.58 (0.57−0.59)
WHO respiratory rate cutpoints and temperature	0.72 (0.70−0.73)
90th percentile respiratory rate, age and temperature stratified	0.61 (0.60−0.62)
95th percentile respiratory rate, age and temperature stratified	0.58 (0.57−0.60)

AUC indicates area under the curve; CI, confidence interval; and WHO, World Health Organization.

*Significantly greater AUC compared to respiratory rate/temperature model ($P < .001$) and respiratory rate/age model ($P < .001$).

each 1°C rise in body temperature; therefore, even over a wide range of temperatures, the effect of temperature on respiratory rate is limited. Additionally, there is considerable variation in respiratory rate within age- and temperature-stratified groups; importantly, the magnitude of this variation exceeds the incremental change in respiratory rate related to temperature change. Despite this significant interpatient variability and limited effect of temperature on respiratory rate, prediction of pneumonia can be enhanced with temperature adjustment of respiratory rates. This improved diagnostic value is even more pronounced when using age-based respiratory rate thresholds for defining pneumonia risk as used by WHO (AUC increased from 0.58 to 0.72).

Illustrative Case

A 2-year-old healthy child presents with fever and cough of 1 day duration. His initial vital signs noted a temperature of 40.1° C, a respiratory rate of 44 breaths/minute, and an oxygen saturation of 97% in room air. Despite the height of fever and tachypnea, the child appears well with clear lungs bilaterally. Physical examination does not identify any localizing signs of infection. Based on respiratory rate alone, should the patient be treated for pneumonia or have a chest radiograph?

Discussion: In an economically developed health care setting, a provider might be tempted to order a chest radiograph but ideally should provide antipyretics and re-evaluate the patient and respiratory rate. If the patient remains tachypneic after fever reduction, a chest radiograph may be indicated to identify pneumonia. In a low-resource setting, this child would be treated with antibiotics for pneumonia based on the presence of cough and respiratory rate >40 breaths/minute; however, with an expected reduction in respiratory rate after treatment with antipyretics (2.6 breaths/minute per degree), the child's respiratory rate would fall below the treatment threshold. Finally, in either health care setting, the same child presenting with a respiratory rate of 56 breaths/minute and a temperature of 40.1°C should be further evaluated (or treated) for pneumonia, as that degree of tachypnea should not be attributed to fever alone.

Respiratory rate is an important finding among patients with lower respiratory tract diseases such as asthma, bronchiolitis, and pneumonia. Physiologically, fever increases respiratory rate and the depth of ventilation in response to increased metabolism and as a cooling mechanism.[9,10] Previous investigations of the influence of temperature on respiratory rate have given mixed results, and some of these studies were performed in adults with external warming[24,25] or in children without illness.[26] In a study conducted in Gambia and based on 370 observations among febrile children less than 5 years of age, Campbell et al[15] observed an increase of 2.5 breaths/minute for each increase of 1°C of fever. In another study by Gadomski et al,[11] 104 febrile children less than 24 months old were randomized to acetaminophen or placebo, and respiratory rates were measured at 1 hour and 1.5 hours. The authors estimated that respiratory rate should be corrected by 5 to 7 breaths/minute for each 1°C (and 7 to 11 breaths/minute for those children less than 12 months of age); the authors also emphasized the variability in respiratory rate measurements as observed in our cohort. In a large study of 14,487 children seen at 2 EDs in the United Kingdom, the relationship between temperature and respiratory rate was explored with quantile regression models, but patients with known respiratory illness were not excluded.[16] The authors concluded that respiratory rates had extreme variability by age and temperature, and they estimated a change between 0.5 and 2.0 breaths/minute for each 1°C increase in temperature.

Respiratory rate has been recognized as an indicator of pneumonia and other lower respiratory tract conditions. Prior studies have shown the limitations of tachypnea as a sole predictor of pneumonia, not surprising given the wide variability of respiratory rates not driven by respiratory disease.[8,27] Two meta-analyses investigating clinical findings of pneumonia found tachypnea (based on WHO criteria thresholds) to have positive likelihood ratios of 1.9 (95% CI, 1.5−2.5)[28] and 1.5 (95% CI, 1.3−1.7).[29] In another investigation of tachypnea to predict pneumonia, Taylor et al[13] defined age-based cutpoints of tachypnea but also noted a relatively small effect of temperature on respiratory rate when pooling measurements due to the extreme variability. In a large observational cohort of 1555 children 1 month to 16 years of age, Nijman et al[12] investigated the relationships among age, temperature, respiratory rate, and lower respiratory tract conditions. This study provided percentile cutpoints for respiratory rate based on temperature and age and also determined that respiratory rate increased 2.2 breaths/minute per 1°C. The authors demonstrated the test performance of temperature/respiratory rate thresholds for any lower respiratory tract illness, but not specifically for pneumonia. Our current study supports a similar modest increase in respiratory rate for elevated temperature as well as the importance of incorporating temperature along with respiratory rate for any risk assessment of pneumonia.

Several limitations should be noted. First, respiratory rates in young children can be affected by anxiety, pain, altitude, respiratory and non-respiratory illness, and state of consciousness; these factors likely led to the variability of respiratory rates noted by age and temperature. We believe that the large study population allowed the investigation of fever and respiratory rate, but the large variation in respiratory rate for any given temperature likely reflects both the physiologic and measurement challenges in young children. Additionally, it is important to acknowledge that the methods of obtaining temperature varied by age, and the measurements are not necessarily interchangeable. In the analysis of respiratory rate as a predictor of pneumonia, we used diagnostic codes of pneumonia without any verifying clinical information. Furthermore, we artificially created a population by reintroducing pneumonia but not other lower respiratory tract conditions; although this facilitated our analysis, the exact prediction of pneumonia would require discrimination from other lower respiratory tract illnesses. Additionally, the importance of respiratory rate as a predictor of pneumonia was only measured in this urban, mostly immunized population and therefore may be different in other populations such as in resource-poor settings. Finally, we paired vital signs taken within 15 minutes of the other parameter, and we did not consider a sensitivity analysis to understand how rapidly temperature or respiratory rate can change over a 15-minute time frame.

CONCLUSIONS

Respiratory rate increases by an average of 2.6 breaths/minute for each 1°C of body temperature among children less than 5 years old. This effect may be difficult to recognize across patients given the significant variability in respiratory rate by age and temperature. Despite this variability, the combination of temperature with respiratory rate improves the prediction of pneumonia over respiratory rate alone and should be considered in care models assessing pneumonia risk.

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Authorship statement: R.G.B. conceived of this study, performed data analyses, drafted the manuscript, and assumed final responsibility for the submitted manuscript. K.A.M. conceived of the study, developed the dataset from hospital information systems, provided guidance in design and analysis, provided critical review of the manuscript, and approved the final version. M.I.N. provided guidance for the design and analysis, provided critical review of the manuscript, and approved the final version. M.C.M. provided guidance for the design, had full access to all data, performed the data analysis, partially drafted the manuscript, provided critical review of the manuscript, and approved the final version.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.acap.2018.11.015.

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