

# Comparison of Procalcitonin With Commonly Used Biomarkers and Algorithms for Evaluating Suspected Pediatric Musculoskeletal Infection in the Emergency Department

Lyndsey van der Laan, MD, MPH,\*† Nakia Gaines, MD,\*† Ngoc Van Horn, MD,\*†  
Chanhee Jo, PhD,‡ Yuhua Ma, MS,‡ and Lawson A. Copley, MD, MBA, FAAOS\*†‡

**Introduction:** It is difficult to distinguish between children with infectious versus noninfectious conditions of the musculoskeletal system during initial evaluation. Clinical predictive algorithms potentially support this effort but not without limitations. Procalcitonin (PCT) has been proposed as a biomarker to help differentiate infection from noninfection. This study evaluates the adoption and utility of PCT during initial infection evaluations and assesses test characteristics of commonly used parameters and algorithms.

**Methods:** PCT was introduced for initial laboratory evaluation of the suspected musculoskeletal infection. Prospective enrollment occurred from July 2020 to November 2021 with 3 cohorts established after a retrospective review of final diagnoses at the end of treatment: 1) deep infection, 2) superficial infection, and 3) noninfection. Univariate and multivariate logistic regression analysis of parameters and diagnoses was performed. Test characteristics of individual and aggregated parameters were assessed.

**Results:** Among 258 children evaluated, 188 (72.9%) had PCT drawn during the evaluation. An increase of PCT acquisition from 67.8% to 82.4% occurred over the study timeframe. Eighty-five children were prospectively studied, including those with deep infection (n=21); superficial infection (n=10), and noninfection (n=54). Test characteristics of parameters showed accuracy ranging from 48.2% to 85.9%. PCT >0.1 ng/mL independently predicted deep infection in 84.7% of cases, outperforming white blood cell, C-reactive protein (CRP), and absolute neutrophil count. Using study thresholds for CRP, erythrocyte sedimentation rate, PCT, and Temp improved accuracy to 89.4%.

**Conclusions:** PCT is a potentially useful biomarker during the initial assessment of children suspected to have a musculoskeletal infection. Systematic evaluation using a combination of parameters improves the accuracy of assessment and assists predictive judgment under uncertainty. PCT <0.1 ng/mL, erythrocyte sedimentation rate

<18 mm/hr, CRP <3.3 mg/dL, and temperature <37.8°C should reasonably reassure clinicians that deep musculoskeletal infection is less likely, given the high negative predictive value and collective accuracy of these parameters.

**Level of Evidence:** Level III – Retrospective cohort comparison

**Key Words:** Procalcitonin, biomarkers, musculoskeletal infection, pediatric

(*J Pediatr Orthop* 2023;43:e168–e173)

Children with signs and symptoms concerning infectious, inflammatory, or reactive conditions involving the musculoskeletal system create a diagnostic dilemma. It is challenging to distinguish between these conditions to establish accurate diagnoses during a single encounter due to the similarity of history, physical findings, and laboratory results. Although unrealistic in deriving final diagnoses from the initial assessment, there is value in rapidly determining, which children should be (1) admitted for further assessment; (2) scheduled for subspecialty evaluation, or (3) allowed to follow-up with primary care physicians or only as needed.

No single laboratory parameter consistently distinguishes infection from similar conditions. This can lead to inaccurate diagnosis and delay in the treatment at one extreme or unnecessary intervention at the other.<sup>1</sup> Clinical prediction algorithms using combinations of risk factors to determine relative probabilities of serious musculoskeletal infections have the potential for error.<sup>2–8</sup> Nonetheless, the advantage of using discrete criteria to establish the relative risk of infection is appealing to simplify early decisions concerning the appropriateness of additional inpatient assessment. There is increasing evidence that decision algorithms reduce noise in healthcare, particularly when uncertainty and diagnostic complexity are encountered because humans have a tendency to be noisy (highly variable) in our evaluations and judgments.<sup>9</sup> However, there are also disadvantages of decision algorithms due to the potential to be misleading when applied to populations that differ from those initially modeled or when applied

From the \*Children's Health System of Texas, Dallas, TX; †University of Texas Southwestern; and ‡Texas Scottish Rite Hospital for Children, Dallas, TX.

The authors declare no conflicts of interest.

Reprints: Lawson A. Copley, MD, MBA, FAAOS, Children's Medical Center Dallas, Dallas 75235, TX. E-mail: lawson.copley@childrens.com

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

DOI: 10.1097/BPO.0000000000002303

to conditions other than that for which they were intended.<sup>9–11</sup>

Procalcitonin (PCT), a precursor of the calcitonin peptide, is produced in the presence of bacterial endotoxins, tumor necrosis factor (TNF)-alpha, and interleukin (IL)-6. Evidence suggests that PCT is minimally produced in viral, reactive, or inflammatory conditions.<sup>12</sup> A previous meta-analysis showed PCT was more accurate than C-reactive protein (CRP) in diagnosing systemic bacterial infections.<sup>13</sup> Despite the widespread use of PCT in adult infections, its utility is less established for children.<sup>14</sup> The purpose of this study is to introduce PCT in the evaluation of children at a tertiary pediatric center and assess adoption among providers. A secondary aim is to evaluate the relative merit and accuracy of clinical prediction algorithms and laboratory parameters, including PCT, during the initial assessment of children with acute presentations concerning musculoskeletal infection. Although this study seeks to define general thresholds of laboratory parameters that may be useful to distinguish infection from noninfection, it is not intended to add yet another prediction algorithm for this purpose.

## METHODS

Following the Institutional Review Board (IRB) approval, children with initial concern for musculoskeletal infection who presented to the institution from July 2020 to November 2021 were prospectively enrolled by informed consent and retrospectively studied after the follow-up. The target for prospective enrollment was ~200, as determined by the average rate of musculoskeletal infection consultations at this institution of 350 to 400 per year. Because PCT technology was just being introduced to the institution, there was no preliminary data for power analysis.

Because of growing interest in PCT for the work-up of sepsis, an institutional decision was made to procure the laboratory capability in April 2020. An order set, including PCT, among other commonly ordered infection labs, was created for use at the ED provider's discretion. Children entered the system through the ED, outpatient clinic, or inpatient admission (inclusive of hospital transfers and direct admission by community pediatricians who contacted the admitting service through the hospital access center). Follow-up evaluation occurred in the orthopaedic outpatient clinic or, when necessary, by telephone contact. After the follow-up, 3 study cohorts were established: 1) deep infection (osteomyelitis, septic arthritis or pyomyositis); 2) superficial or skin structure infection (cellulitis or abscess), or 3) noninfection. Data were retrospectively gathered from the chart review, including history, vital signs, laboratory values, and diagnoses. Temperature recordings performed in the ED or inpatient hospital were reviewed for the entire period of observation (up to 24 hours) to capture the maximum recorded temperature for study purposes. All temperature measurements were done by a temporal artery thermostat or temporal scanner. Children were excluded for symptom duration

≥ 28 days, antibiotic treatment, insufficient follow-up, or if no PCT was obtained.

Statistical analysis of continuous variables was accomplished with ANOVA and Mann-Whitney test. Tukey test was conducted for 2 group comparisons.  $\chi^2$  was used for discrete variables with Fisher exact test for small sample sizes ( $\leq 5$ ). Statistical significance was established at  $P < 0.05$ . Multivariate logistic regression analysis and receiver operating characteristics (ROC) identified parameters and thresholds for the risk of deep infection. Test characteristics of independent variables and common combinations of parameters with historically established thresholds were determined for deep infection versus superficial infection or noninfection.

## RESULTS

### Study Population

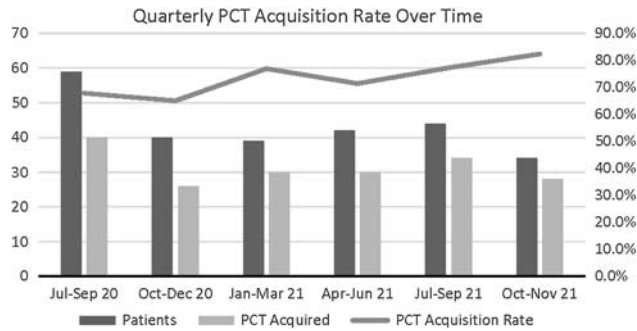
During the study timeframe, 258 children were evaluated for suspected musculoskeletal infection. Among these, 200 (77.5%) were initially assessed in the ED, 36 (14.0%) in the clinic, and 22 (8.5%) after direct admission to the hospital. Of 129 children prospectively enrolled, after exclusion criteria were applied, 85 were categorized into cohorts of 1) deep infection ( $n = 21$ ); 2) superficial infection ( $n = 10$ ), and 3) noninfection ( $n = 54$ ). A chart review was performed for 80 children who had hospital admission or subsequent encounters in the outpatient clinic. Telephone contact was necessary for 5 nonadmitted children who did not follow-up in the clinic. These families each confirmed that their child's symptoms, which prompted the concern, had completely resolved; hence, they did not elect to keep the follow-up appointment. Final diagnoses were determined as viral or reactive arthritis ( $n = 21$ ), trauma ( $n = 16$ ), and self-limited pain ( $n = 12$ ) for noninfection; osteomyelitis ( $n = 17$ ) and septic arthritis ( $n = 4$ ) for deep infection; and cellulitis, abscesses, and septic bursitis for superficial infection ( $n = 10$ ). Hospital admission occurred for 36 of 85 (42.4%) children, including 14 (25.9%) for noninfection, 3 (30.0%) for superficial infection, and 19 (90.5%) for deep infection. Children with deep infection had a significantly higher admission rate than that of the noninfection cohort ( $P < 0.001$ ) and superficial infection cohort ( $P = 0.0013$ ).

### PCT Adoption

Among 258 children, 188 (72.9%) had PCT drawn during their evaluation. There was a progressive increase in PCT acquisition throughout the study period, with PCT acquired for 40 of 59 (67.8%) children during the first quarter. By the final quarter, PCT was acquired for 28 of 34 (82.4%) children (Fig. 1). Systematic acquisition of all parameters, including complete blood count with differential, erythrocyte sedimentation rate (ESR), CRP, and PCT occurred during 187 (72.5%) evaluations.

### Cohort Comparison

There were no significant differences in sex, insurance, ethnicity/race, trauma history, or viral symptoms. Children



**FIGURE 1.** Trend of increasing acquisition of PCT assessed on a quarterly basis during the study period. PCT acquisition improved from 67.8% to 82.4% institutionally over a 17-month timeframe.

with deep infection were significantly differentiated from those with superficial infection by fever, maximum temperature, admission, CRP, ESR, and number of Kocher ± Caird criteria (Tables 1 and 2). Similarly, children with deep infection were differentiated from those with noninfection by fever, tachycardia, white blood cell (WBC) count, absolute neutrophil count, CRP, ESR, number of Kocher ± Caird criteria, and PCT. Children without infection were differentiated from children with superficial infection by age and WBC. PCT significantly differentiated

deep infection (mean of 0.4 ± 0.5 ng/mL) from noninfection (mean of 0.1 ± 0.1 ng/mL) ( $P = 0.0002$ ) (Table 2).

**Multivariate Analysis**

Logistic regression modeling identified significant contributions of maximum recorded temperature and CRP when differentiating cohorts (Table 3). Area under the curve (AUC) was the highest for fever, ESR, CRP, and PCT to differentiate deep infection from the others (Table 4). PCT had a 90.5% sensitivity to identify deep infection.

**Test Characteristics**

The accuracy of parameters ranged from 48.2% (inability to bear weight) to 85.9% (Kocher+Caird ≥ 3 risk factors). PCT > 0.1 ng/mL independently predicted deep infection in 84.7% of cases, outperforming WBC, CRP, and absolute neutrophil count (Table 5). The false positive rate for identification of deep infection was 11.8% when a cutoff of 0.1 ng/mL was used. When using receiver operating characteristics cutoff values for CRP (3.3 mg/dL), ESR (18 mm/hr), PCT (0.1 ng/mL), and temperature (37.8° C), accuracy improved to 89.4%.

**DISCUSSION**

A multi-center study recently reported that 10 percent of pediatric orthopaedic consultations were for musculoskeletal infection and that culture-positive

**TABLE 1.** Discrete Data Comparison Between Children with Non-Infection, Superficial Infection and Deep Infection

Variable	Category	Infection			Overall	Noninfection vs.		Superficial vs. Deep Infection
		Noninfection	Superficial Infection	Deep Infection		Superficial	Deep	
Sex	Female	21 (38.9)	5 (50.0)	6 (28.6)	0.491	0.728	0.438	0.423
	Male	33 (61.1)	5 (50.0)	15 (71.4)	—	—	—	—
Insurance Class	CHIP	2 (3.8)	0 (0.0)	0 (0.0)	0.290	0.330	0.418	0.215
	Commercial	14 (26.5)	3 (30.0)	7 (33.3)	—	—	—	—
	Medicaid	35 (66.0)	5 (50.0)	14 (66.7)	—	—	—	—
	Self Pay	2 (3.8)	2 (20.0)	0 (0.0)	—	—	—	—
Ethnicity; Race	Hispanic; American Indian	1 (1.9)	0 (0.0)	0 (0.0)	0.809	0.711	0.835	0.379
	Hispanic; Other	2 (3.8)	0 (0.0)	1 (4.8)	—	—	—	—
	Hispanic; White or Caucasian	14 (26.4)	3 (30.0)	6 (28.6)	—	—	—	—
	Non-Hisp; Asian	2 (3.8)	0 (0.0)	0 (0.0)	—	—	—	—
	NonHisp; Black/African American	12 (22.6)	2 (20.0)	3 (14.3)	—	—	—	—
	Non-Hisp; Other	3 (5.7)	1 (10.0)	0 (0.0)	—	—	—	—
	Non-Hisp; Unknown	1 (1.9)	1 (10.0)	0 (0.0)	—	—	—	—
	Non-hisp; White/Caucasian	18 (34.0)	3 (30.0)	11 (52.4)	—	—	—	—
Hx Trauma		15 (27.8)	5 (50.0)	4 (19.0)	0.200	0.264	0.560	0.105
Hx Viral Symptoms		12 (22.2)	1 (10.0)	2 (9.5)	0.344	0.672	0.325	1.000
Inability to bear weight		32 (59.3)	6 (60.0)	16 (76.2)	0.628	1.000	0.483	0.417
Fever (≥ 38C) in ED		9 (16.7)	1 (10.0)	17 (81.0)	<0.001	1.000	<0.001	<0.001
Tachycardia		10 (20.8)	3 (30.0)	9 (50.0)	0.069	0.678	0.032	0.434
WBC > 12.0		10 (18.5)	6 (60.0)	11 (52.4)	0.002	0.012	0.008	1.000
ESR ≥ 40		4 (7.4)	0 (0.0)	13 (61.9)	<0.001	1.000	<0.001	0.001
CRP ≥ 2		13 (24.1)	6 (60.0)	19 (90.5)	<0.001	0.053	<0.001	0.067
Hospital Admission		14 (25.9)	3 (30.0)	19 (90.5)	<0.001	1.000	<0.001	0.001

Discrete data comparison between cohorts using  $\chi^2$  and Fisher Exact Test. C indicates Centigrade; CHIP, Children’s Health Insurance Program; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; Hx, History; Non-hisp, Non-Hispanic; PCT, Procalcitonin; WBC, White Blood Cell Count.

**TABLE 2.** Continuous Data Comparison Between Children with Non-Infection, Superficial Infection, and Deep Infection

Variable	NonInfection					Superficial Infection					Deep Infection					Overall Anova P	Noninfection vs. Superficial Infection vs. Deep Infection		
	n	Mean	SD	Min	Max	n	Mean	SD	Min	Max	n	Mean	SD	Min	Max		Superficial Infection	Deep Infection	Deep Infection
Max Temp	46	37.3	0.6	36.4	39.0	10	37.2	0.5	36.4	38.2	18	38.9	0.9	37.1	40.2	<0.001	0.977	<0.001	<0.001
WBC	54	9.7	4.1	4.1	25.3	10	14.3	5.2	8.5	23.8	21	13.5	5.9	6.0	26.4	0.002	0.019	0.009	0.897
ANC	54	4.9	3.7	1.1	18.8	10	7.9	2.2	4.7	11.4	21	9.4	5.1	3.4	21.4	<0.001	0.074	<0.001	0.611
ESR	54	15	13	3	58	10	9	6	1	17	21	44	23	9	92	<0.001	0.489	<0.001	<0.001
CRP	52	1.6	2.8	0.4	14.6	10	4.4	6.9	0.4	23.5	21	9.2	7.8	0.4	28.1	<0.001	0.238	<0.001	0.040
PCT	54	0.1	0.1	0.0	0.9	10	0.2	0.4	0.0	1.3	21	0.4	0.5	0.0	2.0	<0.001	0.617	<0.001	0.119
Kocher Criteria	54	1.0	0.9	0.0	3.0	10	1.2	0.8	0.0	2.0	21	2.6	0.7	1.0	4.0	<0.001	0.687	<0.001	<0.001
Kocher +Caird	54	1.2	1.1	0.0	4.0	10	1.8	0.8	1.0	3.0	21	3.5	0.9	1.0	5.0	<0.001	0.235	<0.001	<0.001

Continuous variable cohort comparison with Analysis of Variance (Anova) and Tukey analysis between groups. ANC indicates Absolute Neutrophil Count; C, Centigrade; CRP, C-Reactive Protein; ED, Emergency Department; ESR, Erythrocyte Sedimentation Rate; max, maximum; min, minimum; PCT, Procalcitonin; Temp, Temperature; WBC, White Blood Cell Count.

confirmation of infection occurred in only 37% of cases.<sup>15</sup> Accurate diagnosis of children with signs and symptoms of musculoskeletal infection is challenging due to the tremendous overlap of symptoms, physical findings, and inflammatory markers between infectious and noninfectious conditions. Daniel Kahneman recently explored the extent to which judgment under uncertainty, particularly predictive judgment, is subject to noise, bias, and objective ignorance in modern healthcare.<sup>9</sup> Within the past 2 decades, there has been a diligent search for strategies to systematically reduce these errors through the formulation of guidelines and decision algorithms.<sup>2-11</sup> Investigators have attempted to apply these algorithms to differentiate infection from other conditions.<sup>2-11</sup> This is necessary not only to reduce diagnostic variability but also to assist human judgment, particularly for providers with less experience. It is a cautionary tale, however, that guidelines and algorithms are potentially misleading and may increase the risk of unnecessary hospitalizations and invasive procedures on 1 extreme or delay in diagnosis and progression of infection on the other.<sup>10,11</sup>

The findings of this study emphasize that parameters and threshold values commonly used for this purpose, individually or in aggregate, all have limitations. It is not surprising that the accuracy was low, ranging from 48.2% to 84.7%. The greatest contribution of the parameters determined in this study was their negative predictive value. As such, providers should generally trust negative results and be reassured that ongoing conservative observation is reasonable in the presence of normal results or whenever the values are well below the cutoff levels, which this study identified.

This study also found that the accuracy of parameters varied based on cutoff values and when multiple parameters were used in combination. However, even with multiple risk factors, the overall accuracy did not exceed 90%. It is, therefore, not the intention of this study to propose yet another algorithm with new thresholds and probabilities. Rather, the purpose is to demonstrate the facility by which PCT was introduced into the systematic work-up for musculoskeletal infection at a tertiary pediatric medical center and its relative merit as a biomarker for infection. PCT appears to value during musculoskeletal infection evaluations, but this study demonstrates its

**TABLE 3.** Logistic Regression Modeling of Deep Infection Versus Non-Infection or Superficial Infection

Logistic Regression Modeling				
Deep Infection versus Superficial Infection or Noninfection				
Variable	Odds Ratio Estimates	95% Wald CI of OR	P	
Max Recorded Temp in ED	0.16	0.46	0.06	0.00
ESR	0.99	1.03	0.96	0.74
CRP	0.88	0.99	0.79	0.03
PCT	0.20	1.05	0.04	0.06

CI indicates Confidence Interval; CRP, C-Reactive Protein; ED, Emergency Department; ESR, Erythrocyte Sedimentation Rate; Max, Maximum; OR, Odds Ratio; PCT, Procalcitonin; Temp, Temperature.

**TABLE 4.** ROC Analysis of Parameters to Predict Deep Infection

ROC Analysis					
Outcome: Deep Infection (Deep Infection vs. Superficial Infection or Noninfection)					
	N	Sensitivity	Specificity	Cutoff	AUC
Max Temp in ED	74	0.89	0.86	37.8	0.934
ESR	85	0.90	0.78	18.0	0.901
CRP	83	0.76	0.84	3.3	0.866
PCT	85	0.90	0.81	0.1	0.852

AUC indicates Area Under the Curve; CRP, C-Reactive Protein; ED, Emergency Department; Max, Maximum; PCT, Procalcitonin; ROC, Receiver Operator Characteristics; Temp, Temperature.

**TABLE 5.** Test Characteristics of Commonly Assessed Parameters to Evaluate Children for Deep Infection

Test Characteristics of Commonly Assessed Parameters, Individually and Combined					
Variable	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
Inability to bear weight	76.2	39.1	29.1	83.3	48.2
Fever $\geq 38.5^{\circ}\text{C}$	81.0	82.8	60.7	93.0	82.4
WBC $\geq 12.0$	52.4	73.4	39.3	82.5	68.2
ESR $\geq 40$	75.0	93.8	75.0	87.0	84.7
Kocher Criteria $\geq 2$	95.2	73.4	54.1	97.9	78.8
CRP $\geq 2.0$	85.7	71.9	50.0	93.9	75.3
Kocher+Caird Criteria $\geq 3$	90.5	84.4	65.5	96.4	85.9
PCT $> 0.10$	90.4	84.4	64.3	94.7	84.7
Admission	90.5	73.4	52.8	95.9	77.6
Temp,CRP $> 3.3$ ,ESR $> 18$ ,PCT $> 0.1$ ( $> 2$ )	81.0	92.2	77.3	93.7	89.4

CRP indicates C-Reactive Protein indicates; ESR, Erythrocyte Sedimentation Rate; NPV, Negative Predictive Value; PPV, Positive Predictive Value; PCT, Procalcitonin; ROC, Receiver Operator Characteristics; Temp, (temperature  $> 37.8^{\circ}\text{C}$ ); WBC, White Blood Cell Count.

limitations, which are similar to that of other commonly used parameters.

PCT has been utilized to diagnose serious bacterial infections in neonates, children, and adults with sepsis and pneumonia.<sup>13,14,16,17</sup> One study showed a PCT cutoff value of 0.2 ng/mL with the sensitivity of 100% and specificity of 94.4% in diagnosing septic arthritis.<sup>18</sup> In our study, PCT of  $> 0.1$  ng/mL had the sensitivity of 90.4%, specificity of 84.4%, and AUC of 0.852 for deep infection. These findings are similar to another study reporting an AUC of 0.72 with cutoff values of PCT  $> 0.1$  ng/mL, ESR  $> 19.5$  mm/hr, and temperature  $> 37.2^{\circ}\text{C}$  being twice as likely to identify musculoskeletal infection.<sup>19</sup> Given limited evidence available to support the use of PCT to assess pediatric infections, the Pediatric Infectious Disease Society guideline for osteomyelitis did not recommend its routine use due to insufficient evidence in its support.<sup>20</sup> Data from our study contribute to the ongoing assessment of PCT for these evaluations. In agreement with the guidelines, our study confirms that more data is needed.

Experience aggregated at this center suggests that a systematic approach is useful to guide decisions during musculoskeletal infection assessments. Providers should conduct a careful history and physical examination and acquire the full panel of initial labs, including complete blood count with differential, CRP, ESR, PCT, and blood culture. While it may seem trivial to mention history and physical examination as part of this systematic approach, the ability to rapidly recognize certain conditions using history and physical findings should not be discounted. This approach minimizes the tendency of parameter-based decision algorithms to overly focus on numerical values or thresholds with less attention to the bigger picture following a comprehensive evaluation of the child.

Laboratory results should be reviewed with mindfulness of the lowest reportable lab value and range of each parameter that might be anticipated in healthy children. These values may differ from 1 reference lab to another, but at our center, they are CRP  $< 0.4$  mg/dL; ESR  $\sim 4$  to 8 mm/hr; and PCT  $< 0.04$  ng/mL. Next, reasonable cutoff or threshold values should be considered to establish a level of concern regarding the relative

magnitude of elevation of the child's labs. With this accomplished, the provider should have an informed intuition regarding the possibility of deep infection. This should guide the decisions for admission and discharge from the ED with planned follow-up in subspecialty clinics, with the primary care physician, or only as needed.

The 72.5% rate of acquisition of all desired laboratory studies and 77.6% rate of admission accuracy are indications that more work is needed to improve these processes at this institution. Providers demonstrate variation in tendencies to order and review a variety of parameters to help with the judgment of infection cases. Given that there are over 40 ED staff at this institution and recognizing that not all providers evaluate patients the same way, the rate of PCT acquisition and admission are enlightening as to the potential challenges to the adoption of these principles at any center.

This study has several limitations. The sample size was smaller than intended during the study design, with enrollment during the peak of the COVID-19 outbreak when ED volumes of viral and bacterial infections were impacted by societal measures of hygiene and social-distancing. This lowered the musculoskeletal infection consultation rate to less than half of the historical average. Another limitation was initial slow enrollment when PCT ordering was not the standard practice. As the adoption of PCT increased at our center, pediatric hospitalists and intensivists have found value in trending PCT in cases of deep infection. A declining PCT enables the recognition of the effectiveness of therapy before the decline of CRP. This is consistent with the findings of other investigators who have reported the benefit of PCT due to its rapid decline in the presence of effective antibiotic treatment.<sup>14,21,22</sup>

## CONCLUSION

PCT is a potentially useful inflammatory marker during the evaluation of children with suspected musculoskeletal infection. A combination of parameters gathered during the systematic assessment of the child appears more helpful in supporting the decision-making and predictive judgment under uncertainty. PCT  $< 0.1$  ng/mL, ESR  $< 18$  mm/hr, CRP  $< 3.3$  mg/dL, and temperature

<37.8°C should reasonably reassure clinicians that deep musculoskeletal infection is less likely, given the high negative predictive value and accuracy of these parameters at the proposed thresholds. For children with a low risk of deep infection, it is more appropriate to consider 1) the outpatient follow-up with a subspecialist for a second look or 2) the follow-up with the primary care physician or as needed. This strategy has been employed at our institution for over 10 years while practicing under guidelines. Annual stakeholder updates are given to ED providers to emphasize that orthopaedic clinic follow-up is appropriate for children sent out from the ED when there is a preliminary musculoskeletal concern but insufficient to warrant admission. The purpose is to allow for additional assessment until a more definitive diagnosis can be determined or, alternatively, spontaneous resolution is reached. An essential lesson of this study is that trending lab values, either in the inpatient or outpatient setting, improve diagnostic accuracy and decision-making over time. Such a practice extends the process of evaluation over hours or days to help differentiate infection from noninfection.

#### REFERENCES

- Pierrie SN, Scannell BP, Brighton BK, et al. Characteristics of Pyogenic musculoskeletal infections in older children and adolescents. *Orthopedics*. 2020;43:e291–e298.
- Kocher MS, Zurakowski D, Kasser JR. Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. *J Bone Joint Surg Am*. 1999;81:1662–1670.
- Kocher MS, Mandiga R, Zurakowski D, et al. Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. *J Bone Joint Surg Am*. 2004;86:1629–1635.
- Caird MS, Flynn JM, Leung YL, et al. Factors distinguishing septic arthritis from transient synovitis of the hip in children. a prospective study. *J Bone Joint Surg Am*. 2006;88:1251–1257.
- Herman MJ, Martinek M. The limping child. *Pediatr Rev*. 2015;36:184–195; quiz 196–7.
- Hwang C. Calculated decisions: Kocher criteria for septic arthritis. *Pediatr Emerg Med Pract*. 2019;16:Cd1–cd2.
- Ryan DD. Differentiating transient synovitis of the hip from more urgent conditions. *Pediatr Ann*. 2016;45:e209–e213.
- Mo M, Guilak F, Elward A, et al. The use of biomarkers in the early diagnosis of septic arthritis and osteomyelitis-A pilot study. *J Pediatr Orthop*. 2022;42:e526–e532.
- Kahneman DSOCR, *Noise: a flaw in human judgement*. 2022.
- Luhmann SJ, Jones A, Schootman M, et al. Differentiation between septic arthritis and transient synovitis of the hip in children with clinical prediction algorithms. *J Bone Joint Surg Am*. 2004;86:956–962.
- Good JJ, Rabener MJ, Fisher GW. Using a decision tool to evaluate for osteomyelitis in children. *Jaapa*. 2021;34:29–32.
- Balog A, Ocsovszki I, Mándi Y. Flow cytometric analysis of procalcitonin expression in human monocytes and granulocytes. *Immunol Lett*. 2002;84:199–203.
- Simon L, Gauvin F, Amre DK, et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis*. 2004;39:206–217.
- Assicot M, Gendrel D, Carsin H, et al. High serum procalcitonin concentrations in patients with sepsis and infection. *Lancet*. 1993;341:515–518.
- Koehler RJ, Shore BJ, Heyworth BE, et al. Defining the volume of consultations for musculoskeletal infection encountered by pediatric orthopaedic services in the United States. *PLoS One*. 2020;15:e0234055.
- Kamat IS, Ramachandran V, Eswaran H, et al. Procalcitonin to distinguish viral from bacterial pneumonia: a systematic review and meta-analysis. *Clin Infect Dis*. 2019;70:538–542.
- Omar J, Isa S, Ismail TST, et al. Procalcitonin as an early laboratory marker of sepsis in neonates: variation in diagnostic performance and discrimination value. *Malays J Med Sci*. 2019;26:61–69.
- Fottner A, Birkenmaier C, Pellengahr C, et al. Can serum procalcitonin help to differentiate between septic and nonseptic arthritis? *Arthroscopy*. 2008;24:229–233.
- McMichael BS, Nickel AJ, Christensen EW, et al. Discriminative accuracy of procalcitonin and traditional biomarkers in pediatric acute musculoskeletal infection. *Pediatr Emerg Care*. 2021;37:e1220–e1226.
- Woods CR, Bradley JS, Chatterjee A, et al. Clinical practice guideline by the pediatric infectious diseases society and the infectious diseases society of America: 2021 guideline on diagnosis and management of acute hematogenous osteomyelitis in pediatrics. *J Pediatr Infect Dis Soc*. 2021;10:801–844.
- Schuetz P, Christ-Crain M, Müller B. Procalcitonin and other biomarkers to improve assessment and antibiotic stewardship in infections—hope for hype? *Swiss Med Wkly*. 2009;139:318–326.
- Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. *BMC Med*. 2011;9:107.