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Original Contributions

CAN A SEPTIC HIP DECISION RULE AID IN THE EVALUATION OF SUSPECTED PEDIATRIC MUSCULOSKELETAL INFECTIONS?

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☐ **Abstract—Background: Musculoskeletal (MSK) infections can be difficult to diagnose in acute care settings. The utility of clinical decision tools for pediatric MSK infections in an emergency department has not been well studied. Objective: Our aim was to evaluate the performance of a septic hip clinical decision rule (CDR) in the evaluation of pediatric musculoskeletal infections. Methods: We performed a retrospective study of children evaluated for an MSK infection in our emergency department from 2014 to 2016. Data collection included demographics, discharge diagnoses, and clinical/laboratory predictors from the CDR. A χ^2 analysis and Wilcoxon rank-sum tests compared patients with and without MSK infections. Logistic regression analysis examined the predictors for MSK infections. A receiver operating characteristic (ROC) curve was calculated to evaluate the performance of the predictors. Results: Of 996 evaluations included in the final analysis, 109 (10.9%) had MSK infections. In a multivariable model, an adjusted odds ratio (OR) was significant for fever (OR 3.9, 95% confidence interval [CI] 2.4–6.4), refusal to bear weight/pseudoparalysis (OR 4.4, 95% CI 2.7–7.1), and C-reactive protein (CRP) > 2.0 mg/dL (OR 5.4, 95% CI 3.2–9.1). The probability of infection was 75.1% with five predictors present, 1.9% for zero predictors, and 5.1% if one predictor was present. An ROC curve showed an area under the curve of 0.82, indicating moderate accuracy. Conclusions: A septic hip CDR demonstrates a low predicted probability of an MSK infection with zero or one clinical predictor present and moderate predictability with all five predictors. Fever, refusal to bear weight/pseudoparalysis, and CRP > 2.0 mg/dL performed best and should alert providers to consider other MSK infections in addition to septic arthritis.** © 2018 Elsevier Inc. All rights reserved.

☐ **Keywords—pediatric; musculoskeletal infection; emergency department**

INTRODUCTION

Musculoskeletal (MSK) infections, such as septic arthritis, osteomyelitis, and pyomyositis are becoming increasingly common. Numerous studies have reported an increased incidence of these infections in the United States and other developed countries are on the rise (1–6). Since 2000, a twofold rate increase in osteoarticular infections and an up to 2.8-fold increase in osteomyelitis have been observed in children (7,8) If these MSK infections are not promptly diagnosed, children can suffer significant morbidity and, in rare cases, mortality (9). Using clinical criteria can aid providers in early recognition and appropriate management to prevent significant morbidity and mortality.

Accurate diagnosis of pediatric MSK infections can be difficult because their clinical presentation varies significantly. In addition, the signs and symptoms of noninfectious processes, such as rheumatic arthritis, oncologic disease, and transient synovitis, can mimic infections.

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Several published studies have attempted to stratify and differentiate individual pediatric MSK infections. Clinical algorithms have been proposed to help differentiate between transient synovitis and septic arthritis of the hip in children based on clinical and laboratory criteria (10–14). In 2014, Copley et al. evaluated a severity scoring system for patients with acute osteomyelitis, but it was limited to data from hospitalized patients and not from emergency departments (EDs) (15). A recent retrospective review proposed a clinical prediction algorithm to differentiate severity of all MSK infections in children presenting to the ED using clinical and laboratory predictors, with authors concluding that an elevated C-reactive protein (CRP), fever, and tachycardia were predictive of severity of infection (16).

Using clinical and laboratory predictors from a septic hip clinical decision algorithm, a care process model for the evaluation and management of children presenting to the ED with suspected MSK infections was implemented in our institution in 2014 (10,11,17). The goal of this study was to examine how these predictors performed in the evaluation of children presenting to an ED for suspected acute MSK infections of either lower or upper extremities.

MATERIALS AND METHODS

Study Design and Setting

This study was a planned secondary analysis of data from a prior retrospective study conducted in a health care system that consists of a free-standing Midwest children's hospital in an urban setting with an annual ED volume of ~65,000, and a free-standing children's hospital in a community setting with an annual ED volume of ~45,000 (17). This study was approved by the health care system's institutional review board.

Selection of Participants

A care process model (CPM) for the evaluation of children presenting to the ED with suspected MSK infections was implemented in April 2014. The CPM provided recommendations on laboratory evaluation, imaging, and subspecialty consultation to aid providers in determining the likelihood of having an MSK infection with guidance on disposition from the ED (17). Patients evaluated for an MSK infection in the ED were first identified using weekly reports generated by an informatics specialist. Reports queried all ED visits between April 15, 2014 and April 30, 2016 that included an electronic order history with either of the following criteria: plain radiograph or ultrasound of a joint or extremity and laboratory evaluation (complete blood count, CRP, and erythrocyte sedimentation rate [ESR]), or magnetic resonance imaging (MRI) of a joint or extremity. Study patients were included for further review if there was provider documentation of concern for MSK infection during the ED evaluation. For this study, we excluded patients < 30 days or ≥ 18 years of age, those with missing data, evaluations involving the hand (defined as distal to the wrist), infections at the site of orthopedic hardware placement within the previous 12 months, fractures or dislocations of the suspected site diagnosed during the ED evaluation, or other diagnoses definitively identified during the ED evaluation, such as leukemia or pneumonia.

Methods of Measurement and Outcome Measures

Electronic medical records were reviewed weekly by the primary investigator, and the data collection was reviewed with the study investigators each week to ensure agreement of all data variables collected (17). Data collection included age, sex, payor type (self-pay, commercial, public), race/ethnicity (white, black, Hispanic, Asian/Pacific Islander, multiracial/other), discharge diagnosis, and the presence or absence of the five clinical and laboratory predictors based on the septic hip clinical decision algorithm: fever > 38.3°C (101°F), non–weight-bearing or pseudoparalysis of the extremity, CRP > 2.0 mg/dL, white blood cell count (WBC) > 12.0×10^9/L, and ESR > 40 mm/h (10,11). The presence of fever was defined as a documented fever > 38.3°C (101°F), measured either by the parent at home or in the ED within 72 h of presentation. Patients who walked with an abnormal gait or limp were considered weight-bearing. For upper extremities, documented provider observation of patient not actively using the affected extremity or joint was used to determine if the patient had pseudoparalysis. Laboratory data were recorded only if laboratory tests were obtained on the day of presentation to the ED. The presence of an MSK infection was defined as an MRI consistent with osteomyelitis, septic arthritis, or pyomyositis, as interpreted by a pediatric radiologist. Additionally, septic arthritis was diagnosed if any of the following was present on evaluation of the joint fluid: grossly purulent aspirate as determined by the orthopedic surgeon, WBC > 50,000/μL, positive culture, or positive polymerase chain reaction. Discharge diagnoses were determined by reviewing provider documentation in the electronic medical record from either ED discharge or hospital discharge documentation. All data variable criteria and definitions were determined and agreed upon a priori by all study investigators.

Data Analysis

Comparisons of patients with and without an MSK infection were performed using χ^2 tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Logistic regression analysis was used to examine the factors

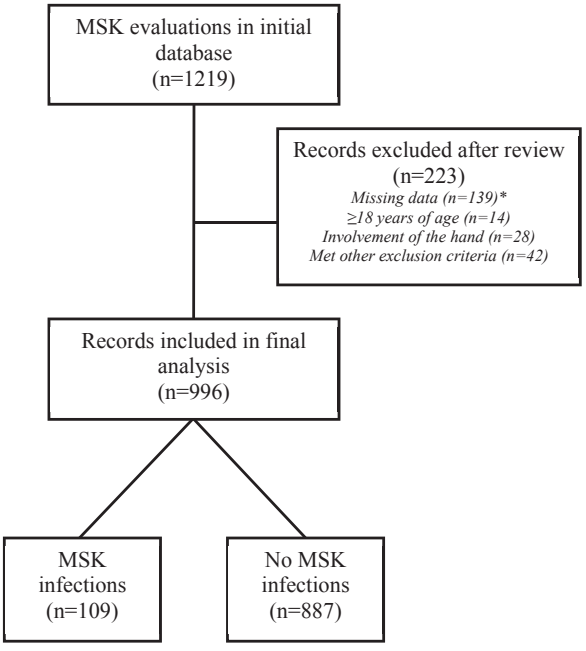

Figure 1. Flow chart of study population. MSK = musculoskeletal.

associated with MSK infections. Adjusted odds ratios and predicted probabilities of an MSK infection are reported. To evaluate the diagnostic performance of the clinical prediction rule in identifying MSK infections, a receiver operating characteristic (ROC) curve with an area under the curve (AUC) was calculated. A significance level of < 0.05 was used for all analyses. Statistical analysis was performed using SAS, version 9.4 (SAS Institute, Cary, NC).

RESULTS

Characteristics of Study Subjects

A total of 1219 evaluations occurred between April 15, 2014 and April 30, 2016, with 996 evaluations included in the final analysis (Figure 1). An MSK infection was identified in 109 (10.9%) children, while 887 (89.1%) did not have an MSK infection. No significant differences were observed in age, sex, payor type, or involvement of the lower extremity among patients with and without an MSK infection. Race was distributed differently between the two groups, with the MSK infection positive group having a larger proportion of white patients ($p < 0.01$) (Table 1). The most common MSK diagnoses were septic arthritis (n = 42 [38.5%]), osteomyelitis (n = 40 [36.7%]), and septic arthritis with osteomyelitis (n = 16 [14.7%]). The most common diagnoses in patients without an MSK infection included pain/swelling/limp not otherwise specified (n = 392 [44.2%]), cellulitis/soft tissue abscess (n = 173 [19.5%]), and transient synovitis (n = 153 [17.2%]) (Table 2).

Main Results

In a univariate analysis, the clinical and laboratory risk factors were all significantly associated with presence of an MSK infection (Table 3). In a multivariable model including all five clinical and laboratory predictors, elevated WBC and ESR were not significantly associated with risk of MSK infection (Table 4). In contrast, fever, refusal to bear weight/pseudoparalysis, and CRP > 2.0 mg/dL had adjusted odds ratios of 3.9 (95% confidence interval [CI] 2.4–6.4), 4.4 (95% CI 2.7–7.1), and 5.4 (95% CI 3.2–9.1), respectively.

The probability that a patient would have an MSK infection was calculated based on the number of predictors present in the ED evaluation. As shown in Table 5, the likelihood of a patient having an MSK infection increased as the number of predictors present increased. The ROC curve for the performance of the predictors is shown in Figure 2. Our study results demonstrate a high sensitivity with a high false-

Table 1. Characteristics of Patients Evaluated for a Suspected Musculoskeletal Infection

Characteristics	MSK Infection Positive (n = 109)	MSK Infection Negative (n = 887)	*p* Value
Age, y, median (IQR)	8.2 (3.3–11.2)	6.1 (3.2–10.8)	0.27
Male, n (%)	72 (66.1)	501 (56.5)	0.06
Payor type, n (%)			
Self pay	2 (1.8)	44 (5.0)	0.10
Commercial	55 (50.5)	368 (41.5)	
Public	52 (47.7)	475 (53.6)	
Race/ethnicity, n (%)			
White	78 (71.6)	455 (51.7)	<0.01
Black	12 (11.0)	215 (24.4)	
Hispanic	7 (6.4)	132 (15.0)	
Asian/Pacific Islander	4 (3.7)	12 (1.4)	
Multiracial/other*	8 (7.3)	66 (7.5)	
Lower extremity involvement, n (%)	99 (90.8)	824 (92.9)	0.43

IQR = interquartile range; MSK = musculoskeletal.
* Other: declined/refused, identified as other, unknown.

Table 2. Diagnoses of Patients Evaluated for Suspected Musculoskeletal Infections

Variable	MSK Infection Positive (n = 109)	MSK Infection Negative (n = 887)
Septic arthritis		
Elbow	1	—
Hip	25	—
Knee	9	—
Ankle/foot	7	—
Osteomyelitis		
Upper extremity	5	—
Pelvis	6	—
Femur	7	—
Lower leg	17	—
Foot	5	—
Septic arthritis + osteomyelitis		
Upper extremity	2	—
Pelvis	3	—
Lower extremity	11	—
Osteomyelitis + pyomyositis		
Upper arm	1	—
Pelvis	1	—
Femur/hip	1	—
Tibia	1	—
Pyomyositis		
Shoulder	1	—
Pelvis	2	—
Thigh	4	—
Pain/limp NOS	—	392
Superficial abscess/cellulitis	—	173
Transient synovitis of hip	—	153
Fracture/injury	—	44
Arthritis*	—	22
Effusion NOS	—	21
Other†	—	82

MSK = musculoskeletal; NOS = not otherwise specified.
* Includes but not limited to: reactive arthritis, Juvenile idiopathic arthritis, arthritis NOS.
† Includes but not limited to: viral illness NOS, Henoch-Schonlein purpura, myositis, bursitis, oncologic, gastrointestinal process.

positive rate when zero predictors are present, as indicated by the cut point in the upper right corner of the graph. Conversely, having five predictors, as seen in the lower left corner, indicated low sensitivity but also a low false-negative rate in determining the presence of an MSK infection. The AUC for our study population was 0.82 (95% CI 0.79–0.86), indicating moderate accuracy in the diagnostic performance. A perfect test would approximate to the upper left corner of the graph with an AUC of 1.0, while random chance would be represented by the diagonal straight line with an AUC of 0.5 (18).

DISCUSSION

To our knowledge, this study is the first to evaluate whether clinical and laboratory predictors for septic arthritis of the hip can aid in the evaluation of children presenting with a suspected MSK infection. Previous studies have reported prediction or classification scores to aid in the evaluation and management of septic arthritis and osteomyelitis, with one recent study proposing a severity classification score for MSK infection in children presenting to an ED (10–16). These studies reviewed patients with known MSK infection diagnoses and did

Table 3. Clinical Predictors Present in Patients Evaluated for a Musculoskeletal Infection

Predictor	MSK Infection Positive (n = 109)	MSK Infection Negative (n = 887)	*p* Value
Temperature > 38.3°C	65 (59.6)	171 (19.3)	<0.01
Refusal to bear weight or pseudoparalysis	73 (67.0)	293 (33.0)	<0.01
C-reactive protein > 2.0 mg/dL	80 (73.4)	198 (22.3)	<0.01
White blood cell count > 12.0 × 10^9/L	45 (41.3)	224 (25.3)	<0.01
Erythrocyte sedimentation rate > 40 mm/h	29 (26.6)	76 (8.6)	<0.01

MSK = musculoskeletal.

Table 4. Multivariable Analysis of Clinical Predictors in Musculoskeletal Infections

Clinical Predictor	Adjusted Odds Ratio	95% Confidence Interval
Temperature > 38.3°C	3.9	2.4–6.4
Refusal to bear weight or pseudoparalysis	4.4	2.7–7.1
C-reactive protein > 2.0 mg/dL	5.4	3.2–9.1
White blood cell count > 12.0 × 10^9/L	1.0	0.6–1.6
Erythrocyte sedimentation rate > 40 mm/h	1.4	0.8–2.6

not include patients with non-MSK infections, which can often be difficult to differentiate in an acute care setting. In this study, we found a higher association of MSK infection with the presence of fever, refusal to bear weight, and elevated CRP. In addition, we observed a lower likelihood of infection when clinical criteria were absent.

Our results also demonstrated the significance of each individual clinical factor in patients with MSK infections compared to those without an MSK infection (Table 3). We further analyzed the clinical criteria to determine the association of each with an MSK infection. Although an elevation in WBC or ESR may indicate inflammation or infection, neither was highly associated by itself with an MSK infection when factoring in the other predictors (Table 4). Both of these markers may be useful in providing a baseline value for further management of the patient's illness or aiding in the diagnosis of non-MSK processes (e.g., leukemia). The presence of a fever, refusal to bear weight or pseudoparalysis, or an elevated CRP demonstrated a higher association with an MSK infection in our study population, consistent with findings from previous studies evaluating septic arthritis, osteomyelitis, and pyomyositis (1,11,15,16,19).

When evaluating how the clinical criteria performed in predicting MSK infection, we observed a greater probability of MSK infection as more clinical factors were present. The initial studies by Kocher and Caird and their colleagues demonstrated a predicted a probability of 97.5–99.6% for septic arthritis of the hip in children when all of the predictors were present (10,11). A 2004 validation study by Kocher et al. showed a slight decrease in differentiation between transient synovitis and septic arthritis in their study population (14). Other validation studies by Luhmann and Sultan and their colleagues demonstrated much lower probabilities (59.1–59.9%) when all predictors were present (12,13). Although a direct comparison to these previous studies would be difficult to make, given that these studies focused on septic arthritis alone, our study demonstrated a 75.1% probability of a suspected MSK infection in children when all 5 predictors were present with an AUC of 0.82, indicating moderate accuracy. In contrast, when zero or one clinical predictor was present, the probability of an MSK infection was relatively low (1.9% and 5.1%, respectively). In the absence of these clinical criteria, our results suggest clinicians should consider other diagnoses and subsequent management strategies for patients presenting with a painful joint or extremity.

Limitations

This study has several limitations. First, due to the retrospective design of the study, all children with a suspected MSK infection evaluated in the ED may not have been included. For instance, patients who did not have radiologic imaging or the recommended laboratory tests ordered within the ED would have been excluded from the initial potential study population. Second, all chart reviews were conducted by a single reviewer who was also part of a multidisciplinary workgroup developing a care process for MSK infection evaluations. Having multiple, trained reviewers with high interrater reliability might have helped minimize bias, but this was not feasible due to limited resources. In order to mitigate this limitation, all of the data collected were reviewed by study

Table 5. Predicted Probability of a Musculoskeletal Infection

No. of Factors	MSK Infection Positive, n (%), (n = 109)	MSK Infection Negative, n (%), (n = 887)	Predicted Probability of MSK Infection, %
0	3 (2.8)	322 (36.3)	1.9
1	18 (16.5)	306 (34.5)	5.1
2	24 (22.0)	150 (16.9)	12.7
3	40 (36.7)	82 (9.2)	28.6
4	14 (12.8)	25 (2.8)	52.3
5	10 (9.2)	2 (0.2)	75.1

MSK = musculoskeletal.

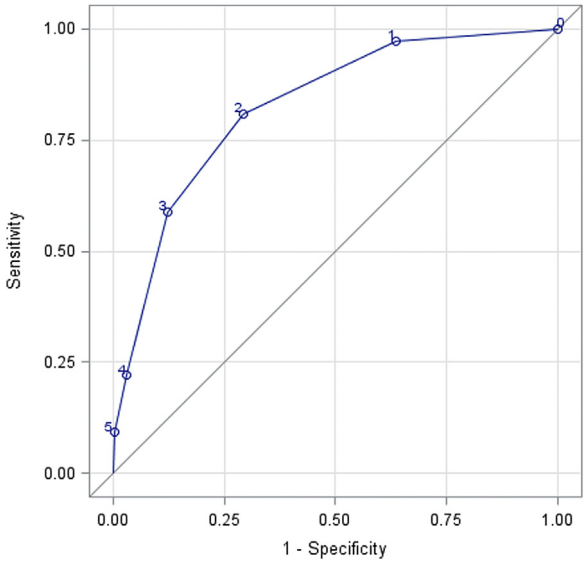

Figure 2. Receiver operating characteristic curve of predictors present in identifying musculoskeletal infections.

investigators on a weekly basis to address any potential discrepancies or questions. Finally, because this study was performed at a single free-standing children's hospital, results might not be generalizable to other children's hospitals or community-based hospitals that care for children.

CONCLUSIONS

In this study, a previously published clinical decision rule for evaluation of pediatric septic hip demonstrated a relatively low predicted probability of an MSK infection in those with either zero or one clinical criterion present and only a moderate predictability with all five predictors. Providers should be cautious and consider the possibility of an MSK infection in patients who present with joint/extremity pain along with presence of a fever, refusal to bear weight/pseudoparalysis, or who have a CRP level > 2.0 mg/dL. Although the presence of the clinical and laboratory criteria can be helpful, consultation with pediatric infectious disease and orthopedic surgery along with access to MRI may be more effective in determining further evaluation and management of children with suspected MSK infections.

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ARTICLE SUMMARY

1. Why is this topic important?

Pediatric musculoskeletal (MSK) infections are becoming increasingly common and are often difficult to diagnose in an acute care setting, such as the emergency department. There are limited studies to aid providers in determining the likelihood of having a MSK infection versus other etiologies for pain in extremities or joints.

2. What does this study attempt to show?

This is a retrospective study evaluating how a previously published clinical decision algorithm for pediatric septic hips performed in children evaluated for suspected MSK infections in an emergency department. Outcomes included predicted probability of a MSK infection based on clinical and laboratory predictors present and the association of individual predictors with MSK infections.

3. What are the key findings?

The presence of fever, refusal to bear weight or pseudoparalysis, and C-reactive protein (CRP) > 2.0 mg/dL were all highly associated with an MSK infection compared to a white blood cell count > 12.0×10^9/L or erythrocyte sedimentation rate > 40 mm/h. There was a relatively low probability of infection when zero or one clinical predictor was present and a moderate predicted probability when all five were present.

4. How is patient care impacted?

Emergency providers should consider other MSK infections in addition to septic arthritis when patients present with a painful extremity or joint in the presence of fever, refusal to bear weight or pseudoparalysis, or CRP >2.0 mg/dL. Although presence of the clinical criteria can be helpful, a clinical algorithm with pediatric subspecialists may be more effective in determining further evaluation and management of these children.