Research article

Generation of a Diagnostic Algorithm that Utilizes ESR and CRP Values in the Detection of Osteomyelitis in Patients with Comorbidities

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Background: **Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests are routinely ordered for differentiating osteomyelitis from cellulitis. However, ESR and CRP values are often overlooked and clinical decisions for diagnosis and treatment of osteomyelitis are primarily based on results of imaging exams. Furthermore, current clinical guidelines do not recommend the use of ESR and CRP as markers for osteomyelitis. Nonetheless, ESR and CRP continue being incorporated in the panel of tests ordered in patients suspected of having osteomyelitis. This practice leads to overutilization and unnecessary testing which can delay proper diagnosis and treatment. In an effort to reduce unnecessary ordering of ESR and CRP tests by providing evidence-based guidelines, this study identified a patient population for which ESR and CRP laboratory values may be clinically significant in detecting osteomyelitis.**

Methods: **A retrospective study from medical records of patients diagnosed with cellulitis and osteomyelitis was completed. Laboratory values of white blood cell (WBC) count, ESR, and CRP were compared between patients presenting with comorbidities and without comorbidities. Optimal cutoff values for ESR and CRP were identified, and a diagnostic algorithm was generated. A second population was utilized to test the performance of the algorithm in differentiating osteomyelitis from cellulitis by utilizing ESR and CRP test results.**

Results: **WBC, ESR and CRP did not provide clinically significant results to identify osteomyelitis in the total patient cohort. However, when grouping patients based on the presence or absence of comorbidities, a cutoff value of > 90 mm/hr for ESR and a value of >10.0 mg/dL for CRP was statistically significant only in the group of patients with comorbidities. Based on the established cutoffs, a diagnostic algorithm was generated which, when tested, demonstrated the ability to correctly identify 97.1% of test patients with a diagnosis of osteomyelitis.**

Conclusion: **The results provide guidelines for the possible better utilization of ESR and CRP when evaluating patients suspected of osteomyelitis. This study suggests the use of a diagnostic algorithm to effectively utilize ESR and CRP test results in a population where the values were demonstrated to be clinically significant.**

Keywords: ESR, CRP, diagnostic algorithm, comorbidities, osteomyelitis, and cellulitis

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Introduction

Accurate and timely diagnosis of osteomyelitis is critical as bone infections are associated with surgeries, amputations, extended exposure to antibiotics, gastrointestinal complications, and acute kidney injury.[1] If osteomyelitis is not properly diagnosed and differentiated from cellulitis, the infection can spread to other parts of the body hence increasing the risk for amputation and septic shock. While the optimal procedure to diagnose osteomyelitis is with bone biopsy results, the practice is not routinely performed due to the invasive nature of the procedure.[2,3] Instead, less invasive methods such as imaging exams, WBC count, ESR, and CRP are the preferred tests for the diagnosis of osteomyelitis.[4,5] However, WBC count, ESR, and CRP are not specific markers for osteomyelitis as they assess overall inflammation regardless of cause.[6–10] Moreover, recommenddations by the Infectious Disease Society of America (IDSA) do not include ESR and CRP testing when evaluating patients for osteomyelitis, rather, the 2012 IDSA Clinical Practice Guidelines suggest the diagnosis of osteomyelitis should be determined by clinical examination and imaging studies.[11]

Despite the IDSA recommendations, ESR and CRP continue being part of the routine testing in the evaluation of patients suspected with osteomyelitis.[12] And, often times, regardless of ESR and CRP values, diagnosticians rely on advanced imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) studies when there is a high index of suspicion for osteomyelitis.[1] Thus, it is important to reassess the diagnostic utility of ESR and CRP when the values are often overlooked and higher diagnostic utility is applied to imaging reports.[12,13]

The practice of discontinuing the use of ESR and CRP for the diagnosis of osteomyelitis may not be immediately possible. Thus, better guidelines can be implemented to improve the clinical utility and continued use when appropriate. Several studies identified ESR and CRP to be of diagnostic utility in diagnosing osteomyelitis of the foot in patients with diabetes.[1,14,15] The variability of ESR and CRP levels observed may be due to the presence of comorbidities or due to other non-infectious inflammatory conditions.[16] Most studies that have evaluated the clinical significance of ESR and CRP have primarily focused on patients with diabetes. Hence, further studies that consider other types of comorbidities are needed to better understand how predisposing conditions may have an impact on the clinical value of ESR and CRP tests.

The purpose of this study was to evaluate the diagnostic utility of ESR and CRP to detect osteomyelitis and determine if there are differences in patient populations that could benefit from the use of the tests. This study is a retrospective analysis of laboratory values from patients diagnosed with cellulitis or osteomyelitis at an academic teaching hospital. ESR and CRP cutoff values to distinguish osteomyelitis from cellulitis in patients with and without comorbidities were established to generate a diagnostic algorithm. Then, a second population was utilized to test the accuracy of the algorithm in identifying patients with osteomyelitis. It is intended that having clear ESR and CRP cutoff values, along with a decision tree, can be an effective method to evaluate patients suspected of osteomyelitis.

Methodology

After obtaining IRB approval (IRB# 23-0013), a non-experimental, quantitative, retrospective, non-blinded study was performed using EPIC to retrieve medical records of patients diagnosed with cellulitis (ICD-10 L03) or osteomyelitis (ICD-10 M86) from January 1, 2018, to December 31, 2022, admitted at an 800-bed academic hospital. Demographic data of age, sex, and race/ethnicity were included to assess relationship on outcome measures. Laboratory values included in the analysis comprised of WBC count, CRP, and ESR values obtained within 72 hours of hospital admission. Comorbidities were defined as patients

presenting with a current or previous diagnosis of cardiac disease (ICD-10 151.9), peripheral vascular disease (ICD-10 173.9), diabetes mellitus (ICD-10 E08), and/or chronic inflammatory disease (ICD-10 G61; K50; K51; J44). Pregnant patients, patients with history of immunosuppressive therapy, autoimmune diseases and immunodeficiencies were excluded as well as patients who did not have an ESR or CRP test performed within 72 hours of admission. Test results for high-sensitivity CRP (hs-CRP) were not included in this study.

A *priori* power analysis and review of previous research was used to determine the appropriate sample size. A two-tailed test with a type I error set at α = 0.05 and a power of 0.95 using *t* test in G*Power software estimated a *priori* sample size of 54 participants for the generation of the algorithm. Contingency tables were created to organize statistical variables that included comparison of factors between patients with cellulitis and with osteomyelitis as well as reliability of WBC, ESR, and CRP for identifying osteomyelitis. Patient demographics and comorbidities were analyzed using Student's *t* test and Mann-Whitney *U* test for continuous variables; x^2 test for homogeneity and Fisher exact test for categorical variables. Receiver operating characteristic (ROC) curve analysis and descriptive statistical analysis were used to determine the performance of WBC, ESR, and CRP tests. Optimal cutoff values were established using maximum Youden's value for WBC, ESR, and CRP in detecting osteomyelitis. Cohen's *d* test was utilized to convert the ROC area under the curve (AUC) value to measure the effect size.[17-19] A *p-value* of ≤0.05 was used to determine the statical significance of the data analyzed.

Results

Establishing the optimal cutoff values for WBC, ESR and CRP

Data from medical records of patients diagnosed with cellulitis or osteomyelitis from January 1, 2018, through June 30, 2022, was used as a data subset to establish optimal cutoff values for WBC, ESR and CRP. A total of 264 patients were identified out of which 127 had a diagnosis of cellulitis and 137 of osteomyelitis (Table 1).

Table 1. Comparison of factors between patients with cellulitis or osteomyelitis. Descriptive statistics were used to calculate frequencies, median values and IQR between 25th and 75th quartiles. Sex, race/ethnicity, and comorbidities are presented for n and percentage of specified group. Percentages are displayed in parentheses. IQR = interquartile range, WBC = white blood cell, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate. *p-value determined using Student's t test and Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables

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Parameter	Total Cohort n = 264		Cellulitis n = 127		Osteomyelitis n = 137		
	Median	IQR	Median	IQR	Median	IQR	*p* value*
Age; median years	61.1	50.050 - 70.025	61.5	49.900 - 71.500	60.8	50.100 - 68.450	0.784
Sex; n (%)							
Male	191	(72.3)	87	(68.5)	104	(75.9)	0.215
Female	73	(27.7)	40	(31.5)	33	(24.1)	0.215
Race/Ethnicity; n (%)							
Caucasian/White	141	(53.4)	71	(55.9)	70	(51.1)	0.460
Black or African American	45	(17.0)	21	(16.5)	24	(17.5)	0.871
Hispanic or Latino	75	(28.4)	33	(26.0)	42	(30.7)	0.416
American Indian or Alaskan Native	2	(0.8)	1	(0.8)	1	(0.7)	1.000
Asian	1	(0.4)	1	(0.8)	0	(0.0)	0.481
Comorbidities; n (%)							
Cardiovascular disease	27	(10.2)	14	(11.0)	13	(9.5)	0.690
Peripheral vascular disease	72	(27.3)	24	(18.9)	48	(35.0)	0.004
Diabetes mellitus	87	(33.0)	22	(17.3)	65	(47.4)	<0.001
Chronic inflammatory disease	10	(3.8)	4	(3.1)	6	(4.4)	0.751
Laboratory values							
WBC (10^3/μL) (baseline)	9.97	7.23 - 13.83	10.69	7.22 - 13.93	9.46	7.21 - 13.75	0.280
CRP (mg/dL)	7.8	2.23 - 16.85	7.8	2.40 - 16.60	7.8	2.00 - 16.95	0.444
ESR (mm/h)	65	40.00 - 99.75	58	31.0 - 91.0	80	46.0 - 107.5	0.001

Age comparison of patients demonstrated no statistically significant difference in age with a total cohort mean age of 61.1 years old. No significant difference in the occurrence of cellulitis and osteomyelitis based on sex was observed. The study population consisted of 53.4% Caucasian/White patients, followed by 28.4% Hispanic/Latino, 17.0% Black/African American, 0.8% American Indian, and 0.4% Asian patients.

Diabetes mellitus was the predominant comorbidity in the total study population with an overall prevalence of 33% followed by 27.3% with peripheral vascular disease, 10.2% with cardiovascular disease, and 3.8% with chronic inflammatory disease. The total study population was categorized to identify patients diagnosed with cellulitis or osteomyelitis presenting with or without comorbidities (**Figure 1**). A total of 49 patients presented with cellulitis and comorbidities, 78 with cellulitis without comorbidities, 94 with osteomyelitis with comorbidities, and 43 with osteomyelitis

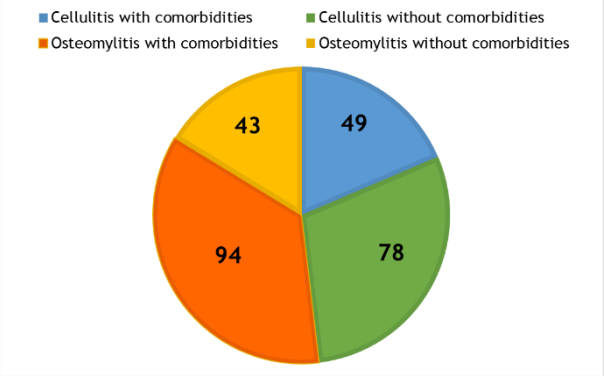
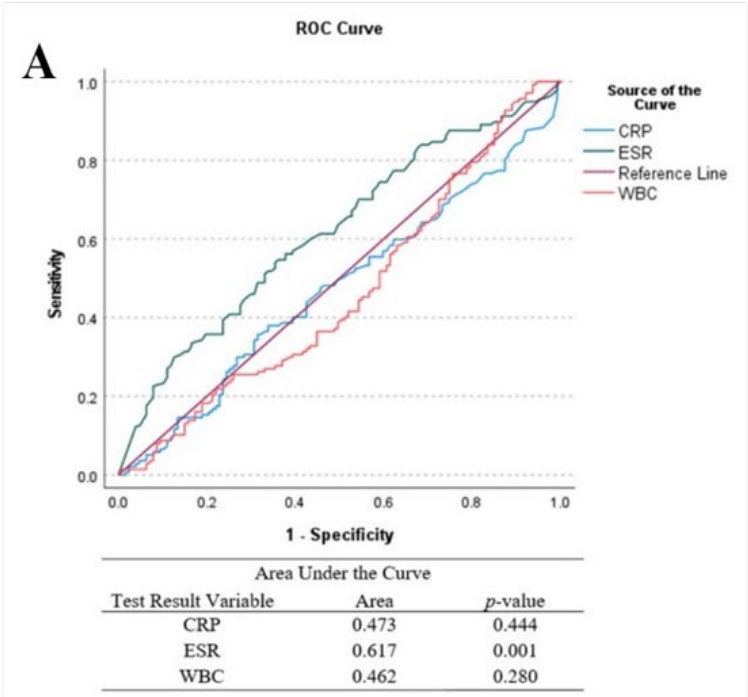


Figure 1. Classification of total cohort of patients. Orange = patients diagnosed with osteomyelitis and comorbidities, green = patients diagnosed with cellulitis without comorbidities, blue = patients diagnosed with cellulitis with comorbidities, and yellow = patients diagnosed with osteomyelitis without comorbidities.

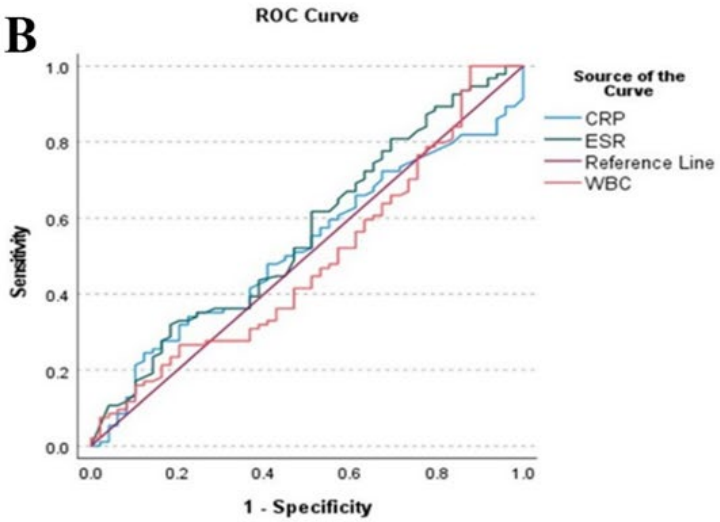
ROC curves were used to determine test performance of WBC, CRP, and ESR in the total cohort, patients with comorbidities, and patients without comorbidities (**Figure 2**). In the total cohort which included patients with and without comorbidities (**Figure 2A**), ESR gave a sensitivity of 61.7% (95% CI 55.0-68.5). The AUC was converted to Cohen's *d* giving a small effect size for ESR.[17] CRP and WBC gave overall sensitivities of 47.3% (95% CI 40.3-54.2) and 46.2% (95% CI 39.1-53.2), respectively. For CRP and WBC, the AUC was below 0.5 and therefore provided no discriminatory ability in detecting osteomyelitis. The ROC in the patients with comorbidities group (**Figure 2B**) showed ESR to have an overall sensitivity of 56.1% (95% CI 46.1-66.1). This converted to Cohen's *d* gave a small effect size of 0.217.[17] CRP and WBC gave overall sensitivities of 51.9% (95% CI 42.3-61.6) and 48.6% (95% CI 38.5-58.8), respectively. The AUC was calculated for CRP and converted to Cohen's *d* gave a negligible effect size of 0.067. The AUC for WBC had no discriminatory ability as it was below 0.5 and the effect size could not be evaluated. For the group of patients without comorbidities (**Figure 2C**), the ESR had an overall sensitivity of 61.2% (95% CI 49.7-72.6) which converted to Cohen's *d* gave a small effect size of 0.402. CRP and WBC gave overall sensitivities of 45.0% (95% CI 34.0-56.1) and 44.1% (95% CI 33.6-54.7), respectively. The AUC of CRP and WBC had no discriminatory ability to differentiate osteomyelitis from cellulitis in patients with comorbidities as they were below 0.5.

Contingency tables were created to detect optimal cutoff values for WBC, ESR, and CRP. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive and negative likelihood ratios (LR+ and LR-), odds ratios, and 95% CI were established for the total cohort (**Table 2**), patients with comorbidities (**Table 3**), and patients without comorbidities (**Table 4**). In the total cohort, an ESR value of >70 mm/hr gave an overall sensitivity of 70.2% with a specificity of 50.0%. However, WBC and CRP performed poorly. In patients with comorbidities, odds ratios and 95% CI demonstrated an ESR level of > 90 mm/hr and CRP level of > 10.0 mg/dL to have the greatest values for detecting osteomyelitis in patients with comorbidities. For patients without comorbidities, the data calculated did not provide significant results in establishing optimal cutoff to differentiate osteomyelitis from cellulitis. Similarly, WBC count could not



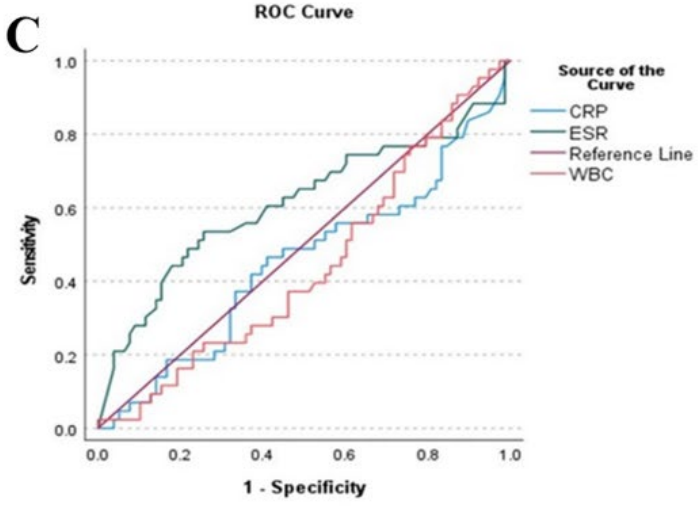
Area Under the Curve

Test Result Variable	Area	*p*-value
CRP	0.473	0.444
ESR	0.617	0.001
WBC	0.462	0.280



Area Under the Curve

Test Result Variable	Area	*p*-value
CRP	0.519	0.694
ESR	0.561	0.230
WBC	0.486	0.793



Area Under the Curve

Test Result Variable	Area	*p*-value
CRP	0.450	0.379
ESR	0.612	0.056
WBC	0.441	0.275

Figure 2. Receiver operating characteristic (ROC) curves for C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell (WBC) count to detect osteomyelitis. A) Total cohort. B) Patients with comorbidities. C) Patients without comorbidities.

provide significant values for establishing cutoff values in any of the groups. The results from the contingency tables were used to construct an algorithm based on the presence or absence of comorbidities and utilizing ESR and CRP values for the detection of osteomyelitis (**Figure 3**).

Testing the performance of the diagnostic algorithm

A second population of 35 patients diagnosed with osteomyelitis or cellulitis from July 1, 2022, to December 31, 2022, was utilized to test the accuracy of the generated algorithm. A two-tailed test with a type I error set at $\alpha = 0.05$ and power of 0.95 in G*Power software demonstrated the study population of 35 patients to meet the minimum effect size criteria with a power of 81.65%. Each of the 35

patients was individually tested by following the algorithm guidelines in which presence or absence of comorbidities defined the need to look up associated ESR or CRP values. If ESR value was > 90 mm/hr, CRP test results were evaluated in which values > 10.0 mg/dL indicated a diagnosis of osteomyelitis. The patient classification by the algorithm was compared to the actual medical records and final diagnosis notes. Following this approach, 34 of the 35 patients tested were correctly identified by the algorithm (**Table 5**). The patients tested had an even representation across ESR and CRP values as well as both patient groups with and without comorbidities were represented.

Table 2. Diagnostic reliability of WBC, ESR, and CRP values for distinguishing osteomyelitis from cellulitis in total cohort including patients with and without comorbidities. WBC = white blood cell; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; OR = odds ratio; CI = confidence interval.

Parameter	Sensitivity	Specificity	PPV	NPV	LR+	LR-	OR	95% CI
Laboratory value:								
WBC (x10^3/μL)								
>10	0.443	0.442	0.473	0.452	0.892	1.211	0.887	0.310 - 0.575
>15	0.529	0.444	0.513	0.517	1.043	0.929	1.140	0.350 - 0.708
>20	0.528	0.444	0.529	0.526	1.125	0.9	1.106	0.095 - 0.960
ESR (mm/hr)								
>20	0.223	0.385	0.375	0.341	0.600	1.733	0.716	0.000 - 0.458
>30	0.547	0.458	0.537	0.527	1.163	0.897	1.028	0.272 - 0.822
>40	0.536	0.583	0.545	0.538	1.163	0.838	1.063	0.320 - 0.753
>50	0.667	0.545	0.579	0.590	1.375	0.698	1.223	0.439 - 0.894
>60	0.698	0.250	0.609	0.563	1.556	0.778	1.321	0.483 - 0.914
>70	0.702	0.500	0.600	0.593	1.464	0.686	1.251	0.405 - 1.000
>80	0.450	0.500	0.466	0.470	0.875	1.071	0.911	0.195 - 0.705
>90	0.618	0.516	0.581	0.607	1.388	0.646	1.046	0.497 - 0.740
CRP (mg/dL)								
>1.0	0.491	0.522	0.497	0.502	0.990	0.994	0.905	0.326 - 0.655
>3.0	0.509	0.400	0.517	0.535	1.071	0.868	1.115	0.278 - 0.740
>6.0	0.480	0.600	0.444	0.444	0.800	0.667	0.148	0.070 - 0.890
>7.0	0.595	0.444	0.563	0.559	1.286	0.788	3.173	0.306 - 0.885
>8.0	0.580	0.667	0.556	0.571	1.250	0.750	2.103	0.337 - 0.823
>10.0	0.599	0.618	0.569	0.550	1.321	0.773	1.289	0.400 - 0.799
>15.0	0.369	0.333	0.420	0.430	0.724	1.324	0.676	0.112 - 0.626
>20.0	0.497	0.500	0.478	0.490	0.914	1.036	0.988	0.324 - 0.670

Table 3. Diagnostic reliability of WBC, ESR, and CRP values for distinguishing osteomyelitis from cellulitis in patients with comorbidities. WBC = white blood cell; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; OR = odds ratio; CI = confidence interval.

Parameter	Sensitivity	Specificity	PPV	NPV	LR+	LR-	OR	95% CI
Laboratory value:								
WBC (x10^3/μL)								
>10	0.465	0.444	0.487	0.455	0.926	1.200	1.053	0.685 - 1.619
>15	0.587	0.625	0.552	0.529	1.204	0.857	0.851	0.573 - 1.265
ESR (mm/hr)								
>20	0.565	0.571	0.534	0.545	1.130	0.818	0.967	0.837 - 1.117
>40	0.539	0.545	0.520	0.514	1.083	0.941	0.977	0.864 - 1.105
>70	0.429	0.286	0.483	0.439	0.933	1.167	1.072	0.866 - 1.329
>90	0.632	0.500	0.581	0.607	1.385	0.586	0.943	0.881 - 1.009
CRP (mg/dL)								
>1.0	0.536	0.500	0.530	0.523	1.089	0.897	1.138	0.287 - 4.519
>3.0	0.607	0.571	0.565	0.560	1.275	0.786	0.685	0.281 - 1.671
>7.0	0.538	0.500	0.530	0.550	1.094	0.821	0.735	0.281 - 1.919
>10.0	0.753	0.700	0.667	0.636	1.613	0.571	0.690	0.486 - 0.980
>20.0	0.400	0.400	0.435	0.444	0.769	1.202	1.039	0.946 - 1.141

Table 4. Diagnostic reliability of WBC, ESR, and CRP values for distinguishing osteomyelitis from cellulitis in patients without comorbidities. WBC = white blood cell; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; OR = odds ratio; CI = confidence interval.

Parameter	Sensitivity	Specificity	PPV	NPV	LR+	LR-	OR	95% CI
Laboratory value:								
WBC (x10^3/µL)								
>10	0.378	0.440	0.417	0.429	0.714	1.328	1.393	0.755 - 2.570
>15	0.392	0.474	0.438	0.435	0.768	1.299	1.032	0.888 - 1.198
ESR (mm/hr)								
>20	0.403	0.556	0.429	0.470	0.750	1.129	1.093	0.762 - 1.568
>40	0.438	0.500	0.471	0.455	0.873	1.100	1.027	0.853 - 1.237
>60	0.458	0.583	0.382	0.467	0.619	1.143	1.166	0.617 - 2.203
>70	0.556	0.444	0.529	0.571	1.125	0.750	0.975	0.816 - 1.164
>90	0.570	0.500	0.533	0.550	1.146	0.819	0.974	0.910 - 1.041
CRP (mg/dL)								
>1.0	0.424	0.444	0.360	0.471	0.563	1.125	1.593	0.238 -10.654
>3.0	0.385	0.462	0.421	0.457	0.731	1.192	1.738	0.396 - 7.624
>7.0	0.273	0.455	0.157	0.397	0.229	1.519	6.331	0.257-155.746
>10.0	0.486	0.563	0.506	0.504	1.026	0.971	1.009	0.813 - 1.250
>20.0	0.533	0.474	0.504	0.503	1.018	0.990	0.992	0.903 - 1.089

Table 5. Performance of the proposed diagnostic algorithm in identifying patients with osteomyelitis. Percentages are displayed in parenthesis. ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.

	Comorbidities n = 12		No Comorbidities n = 23		Met Algorithm Requirements n = 34		Failed Algorithm Requirements n = 1	
Laboratory value, n (%)								
ESR < 40 mm/hr	3	(8.6)	5	(14.3)	7	(20.0)	1	(2.9)
ESR 40 - 90 mm/hr	3	(8.6)	9	(25.7)	12	(34.3)	0	(0)
ESR > 90 mm/hr	6	(17.1)	9	(25.7)	15	(42.9)	0	(0)
CRP ≤ 10.0 mg/dL	4	(11.4)	11	(31.4)	15	(42.9)	0	(0)
CRP > 10.0 mg/dL	8	(22.9)	12	(34.3)	20	(57.1)	0	(0)
Overall algorithm performance, n (%)					34	(97.1)	1	(2.9)

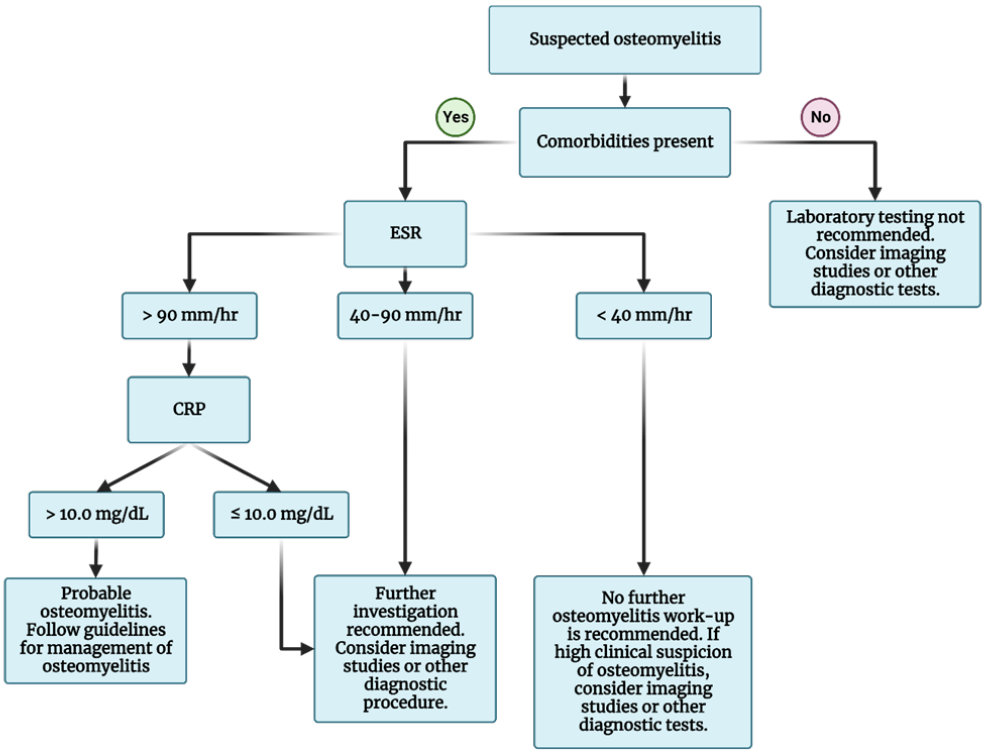


Figure 3. Proposed diagnostic algorithm for the recommended approach to utilizing ESR and CRP in the diagnosis of osteomyelitis. Graphic designed with Biorender.com. ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.

Discussion

In order to establish clear guidelines for the proper utilization of laboratory tests, cutoff values for ESR and CRP were evaluated by comparing patients that present comorbidities and those without. When evaluating ESR and CRP results from the total cohort in detecting osteomyelitis, ESR demonstrated fair performance when > 70 mm/hr and CRP performed poorly at all interval values which correlates with previous studies that report the diagnostic limitations of ESR and CRP tests.[20] However, after the total cohort patient population was grouped into those that present comorbidities (cardiac disease, peripheral vascular disease, diabetes mellitus, or chronic inflammatory disease) and those who do not present comorbidities, the ROC AUC demonstrated ESR to be able to detect osteomyelitis in the patients with comorbidities group only. Likewise, using contingency tables, the diagnostic reliability of ESR and CRP for distinguishing osteomyelitis from cellulitis was found to be statistically significant when ESR > 90 mm/hr and CRP > 10.0 mg/dL in the group of patients that presented comorbidities.

Having clear cutoff values for non-specific inflammatory markers can improve patient outcomes. Based on an evaluation of the current literature, the diagnostic value of establishing cutoff values for ESR and CRP improved patient outcomes. In the diagnosis of periprosthetic infection, ROC analysis and contingency tables demonstrated ESR and CRP to have a sensitivity of 94.3% and 91.1% respectively when an ESR threshold of 30 mm/hr and a CRP cutoff of 10 mg/L were used.[21] In another study, an ESR specific cutoff of 25-30 mm/hr was shown to be useful in the assessment of systemic lupus erythematosus (SLE).[22] Likewise, a CRP cutoff value of > 20 mg/dL was utilized as a risk factor indicator for septic arthritis in children.[23] It is indicated that when used appropriately, ESR and CRP can be highly effective at detecting certain conditions.

Based on the cutoff values obtained from this study, a diagnostic algorithm to detect osteomyelitis was created to guide the diagnostician in selecting appropriate testing by taking into consideration the presence or absence of comorbidities. This algorithm was able to correctly identify 97.1% of the subjects as diagnosed with osteomyelitis. The study presented here appears to be the first to propose a diagnostic algorithm detailing the use of ESR and CRP for the identification of osteomyelitis associated with the presence of comorbidities.

The data presented in this study suggest that patients without comorbidities do not benefit from having an ESR or CRP test performed. Only patients with comorbidities should have an ESR test completed, and if results are greater than 90 mm/hr, follow up with a CRP test, in which only a value >10 mg/dL would suggest osteomyelitis. This is in agreement with other studies that demonstrated ESR and CRP to have little diagnostic utility in detecting osteomyelitis of the foot in nondiabetic patients, but in the case of patients with diabetes, an ESR > 60 mm/hr and CRP > 7.9 mg/dL were found to be optimal cutoff values to initiate treatment for osteomyelitis.[1]

Having clear cutoff values along with an algorithm can benefit diagnosticians in making clinical decisions and reduce overutilization of laboratory tests. As an example, the London Health Sciences Center (LHSC), a tertiary-care hospital located in Ontario, Canada, implemented an educational bulletin and a clinical decision support system to decrease by 40% unnecessary ESR testing which translated to a cost savings of $11,000 Canadian Dollars (CAD) per year.[12]

Similar approaches that derive from utilizing statistical methods such as ROC and contingency tables should be further explored when defining cutoff values. Likewise, establishing specific values or thresholds should be determined for laboratory tests and include consideration of the patients' conditions. The results presented herein suggest that patient comorbidities should be considered before

ordering ESR and CRP test. Ultimately, a diagnostic approach that derives from evidence-based medicine will lead to improved guidelines that can improve health care costs and improve health outcomes.[24]

Limitations

One of the major limitations of this study is the use of retrospective data. In addition, the study population is limited to patients admitted to a single institution. A more comprehensive study should be completed with data from multiple clinical sites. Prior treatment and the use of anti-inflammatory drugs at the time of admission was not evaluated which may have affected baseline ESR and CRP levels.

Conclusion

The results from this study suggest that ESR and CRP are not useful in the diagnosis of osteomyelitis in the general population of hospitalized patients suspected of having osteomyelitis. However, when comorbidities are taken into consideration, ESR and CRP can have clinical value as indicators of osteomyelitis. An improvement in guidelines for the use of ESR and CRP such as the diagnostic algorithm proposed here can help diagnosticians make practical use of the tests and emphasize cutoff values when diagnosing osteomyelitis.

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Institutional Review Board Statement

The Institutional Review Board (IRB) at our institution reviewed this study and determined the project to be a quality assessment/quality improvement study that met the criteria for exemption from review or oversight (IRB #23-0013).

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