The Diagnosis of Osteomyelitis in Diabetes Using Erythrocyte Sedimentation Rate

A Pilot Study

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Osteomyelitis secondary to diabetic foot infections can lead to proximal amputation if not diagnosed in a timely and accurate manner. The authors have found no studies to date that correlate a specific erythrocyte sedimentation rate with osteomyelitis. A retrospective chart review of 29 diabetic patients admitted to the hospital with diagnoses of osteomyelitis or cellulitis of the foot during a 1-year period was performed. Of the various lab values and demographic factors compared, erythrocyte sedimentation rate was the only measure that differed significantly between the two groups. A receiver operating characteristic curve was used to obtain the optimal cutoff value of 70 mm/h, a level above which osteomyelitis was present with the highest sensitivity (89.5%) and highest specificity (100%), along with a positive predictive value of 100% and a negative predictive value of 83%. This study shows that in combination with clinical suspicion in diabetic foot infections, the erythrocyte sedimentation rate is highly predictive of osteomyelitis, and that the value of 70 mm/h is the optimal cutoff to predict accurately the presence or absence of bone infection. (J Am Podiatr Med Assoc 91(9): 445-450, 2001)

Lower-extremity amputations secondary to diabetic pedal infections are the cause of more than 50% of nontraumatic amputations in the United States.[1] In a vast majority of these cases, the underlying cause of amputation is osteomyelitis. Once the diagnosis of osteomyelitis has been made, treatment options include sustained use of intravenous antibiotics or amputation of the infected bone.[2] Accurate and timely diagnosis of osteomyelitis is extremely important to prevent proximal migration of the infection.

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Several different modalities have been advocated for use in the diagnosis of osteomyelitis, including computed tomography, magnetic resonance imaging (MRI), and triple-phase bone scans, all with varying degrees of sensitivity and specificity.[3] Grayson et al[4] proposed that such imaging modalities were not cost-effective and suggested that clinical signs of infection, coupled with the findings of the wound probing to bone, were equally as sensitive and specific while being much more cost-effective to the patient. Bone biopsy, however, remains the gold standard by which all other modalities are compared.[5]

Laboratory tests such as white blood cell count, erythrocyte sedimentation rate, and C-reactive protein have been proposed to aid in the diagnosis of osteomyelitis. In patients with diabetes, however, their response in the presence of infection has been questioned.[6, 7] The erythrocyte sedimentation rate is a simple and inexpensive laboratory test used to assess the body's inflammatory or acute-phase response to disease after the first 24 hours.[8, 9] Fahraeus first described the erythrocyte sedimentation rate in 1918, when he discovered erythrocytes settled more rapidly in pregnant women.[10] The erythrocyte sedimentation rate measures the distance in millimeters that erythrocytes fall in a tube of anticoagulated blood during one hour.[11] The reference range in healthy adults under 50 years old is 0 to 15 mm/h for men and 0 to 20 mm/h for women and is slightly elevated in the elderly population. Several factors have demonstrated an ability to influence the sedimentation rate, including age, sex, pregnancy, anemia, extreme leukocytosis, and protein abnormalities. Furthermore, medical conditions that elevate fibrinogen levels, such as diabetes mellitus, end-stage renal disease, heart disease, collagen vascular disease, and malignancy, have been linked to elevated sedimentation rates (Table 1).[12]

Several authors have reported using the erythrocyte sedimentation rate to aid in the evaluation of various diseases.[9, 11-13] Although it is a strong indicator of inflammation, its clinical usefulness has been questioned due to its low specificity.[8] Some researchers have tried to find a correlation between an elevated erythrocyte sedimentation rate and osteomyelitis, but few have dealt specifically with the diabetic population, which tends to demonstrate a compromised systemic response to infection.[14-16]

In an attempt to correlate an erythrocyte sedimentation rate value in which the presence of osteomyelitis can reasonably be predicted, the authors compared laboratory data from diabetic patients with localized cellulitis to those with confirmed osteomyelitis secondary to foot infections. Since factors such as hyperfibrinogen, renal disease, anemia, age, and sex affect erythrocyte sedimentation rate levels, these factors were evaluated in both patient populations in order to assess their influence.

Materials and Methods

The authors retrospectively reviewed the records of diabetic patients with a diagnosis of either cellulitis or osteomyelitis of the foot admitted to the Illinois Masonic Medical Center in Chicago, Illinois, from December 1, 1998, to December 1, 1999. All of the patients included in the study were required to have had an erythrocyte sedimentation rate level drawn during their hospital stay. A total of 29 patients who met the criteria were included in the study. Pathologic reports were used to confirm the diagnosis of osteomyelitis in all of the patients who underwent an amputation. Pathologic criteria included focal necrosis, intramedullary fibrosis, and extensive reactive and reparative changes.

The presence of osteomyelitis in patients treated conservatively with 6 to 8 weeks of intravenous antibiotics was confirmed with positive results of at least two imaging modalities (bone scan, MRI, radiographs) or the ability to probe an open wound to bone.[4] The diagnosis of cellulitis was confirmed by correlating clinical signs of infection with positive wound cultures. The diagnosis of diabetes mellitus was confirmed using criteria established by the World Health Organization.[17] The hemoglobin, hematocrit, and creatinine obtained on the same day as the erythrocyte sedimentation rate, along with the patients' age and gender, were evaluated to assess if any relationship existed between these variables and the sedimentation rate. The erythrocyte sedimentation rate was obtained using the modified Westergren method. Data analysis included sensitivity, specificity, and positive and negative predictive value for the cellulitis and osteomyelitis groups. A receiver operating characteristic (ROC) curve was obtained to determine the erythrocyte sedimentation rate that maximized the sensitivity value. In addition, a Student's *t*-test, logistic regression, and regression analysis were performed to determine any differences in the variables between the two groups, as well as the effect each variable had on the erythrocyte sedimentation rate.

Table 1. Factors Influencing Erythrocyte Sedimentation Rate (ESR)

Increase ESR	Decrease ESR	No Significant Effect
Old age	Corticosteroids	Obesity
Female	Protein abnormalities	Body temperature
Pregnancy	Sickle cell disease	Aspirin
Anemia	Technical factors	Nonsteroidal anti-inflammatory drugs
Technical factors		
Elevated fibrinogen level		

Results

Twenty-nine patients who met the study's criteria were included in the study. Patient data are listed in Table 2 and the characteristics of the patient population are shown in Table 3. Of the 19 patients with osteomyelitis, pathology reports were used to confirm the diagnosis of osteomyelitis in 10 patients while all of the others were confirmed with at least two different modalities.

There was a significant difference in the mean erythrocyte sedimentation rate between the cellulitis and osteomyelitis groups ($P < .001$). The osteomyelitis group demonstrated a mean erythrocyte sedimentation rate of 104 mm/h while the cellulitis group had a mean erythrocyte sedimentation rate of only 44 mm/h (Fig. 1). Of the variables tested in the two groups, the erythrocyte sedimentation rate was the only clinical measure that differed significantly between the groups (Table 4). This result was further validated by the nonparametric test, the Mann-Whitney test, which also concluded that the only variable that differed between the two groups was the sedimentation rate. When Spearman's rho correlation was used to determine any relationships among the variables tested, the erythrocyte sedimentation rate demonstrated a negative association with hematocrit ($P = .022$) and hemoglobin ($P = .047$). In addition, there was a "trend" significance between gender and hemoglobin ($P = .06$). A stepwise logistic regression analysis of diseased outcome demonstrated that the erythrocyte sedimentation rate was the most significant predictor of osteomyelitis ($P = .007$, $B = .075$) with respect to the other clinical measures. Table 5 presents the sensitivity and specificity of erythrocyte sedimentation rate at five different cutoff levels, along with the ROC curve in Figure 2. An erythrocyte sedimentation rate value equal to or greater than 70 mm/h was the optimal cutoff, with the highest sensitivity (89.5%) and highest specificity (100%) for the presence of os-

Table 2. Patient Data Chart

Patient	Diagnosis	Sex	Hb	Hct	Creatinine	Age	ESR
1	Osteomyelitis	M	11.9	35.9	0.8	54	110
2	Osteomyelitis	F	8.0	27.3	2.2	83	31
3	Osteomyelitis	M	13.2	40.9	1.4	53	40
4	Osteomyelitis	F	10.0	32.4	1.3	71	126
5	Osteomyelitis	M	8.1	24.9	0.9	38	140
6	Osteomyelitis	F	10.1	29.1	1.4	56	140
7	Osteomyelitis	F	7.9	24.2	1.5	61	100
8	Osteomyelitis	F	10.5	32.2	0.8	70	135
9	Osteomyelitis	M	9.3	28.4	1.6	69	93
10	Osteomyelitis	M	10.1	28.4	0.9	51	123
11	Osteomyelitis	M	12.5	40.3	0.7	46	76
12	Osteomyelitis	M	13.3	39.8	1.1	69	73
13	Osteomyelitis	M	10.2	31.5	1.5	48	115
14	Osteomyelitis	F	11.9	35.3	3.1	71	125
15	Osteomyelitis	F	8.8	28.3	1.2	58	95
16	Osteomyelitis	M	11.5	34.8	1.3	55	98
17	Osteomyelitis	M	14.0	39.8	0.7	50	113
18	Osteomyelitis	F	9.9	31.0	1.1	61	132
19	Osteomyelitis	M	13.6	40.7	2.1	53	116
20	Cellulitis	M	14.8	43.0	0.8	65	14
21	Cellulitis	M	10.0	29.7	1.3	41	55
22	Cellulitis	F	11.9	36.8	1.0	76	44
23	Cellulitis	F	13.7	40.7	0.7	83	32
24	Cellulitis	F	10.8	34.2	1.9	92	69
25	Cellulitis	M	11.9	37.2	1.4	70	47
26	Cellulitis	M	11.4	35.3	1.9	84	51
27	Cellulitis	M	10.4	30.7	1.1	66	50
28	Cellulitis	F	11.1	35.3	2.6	56	42
29	Cellulitis	M	12.4	37.8	1.7	47	30

Abbreviations: ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit.

Table 3. Patient Population

Diagnosis	Number of Patients	Gender (male/female)	Age ± SD
Osteomyelitis	19	11/8	58.8 ± 11.0
Cellulitis	10	6/4	68.0 ± 16.5

teomyelitis. It also had the highest predictive value of 100% and negative predictive value of 83%.

Discussion

This investigation represents the first study validating the use of the erythrocyte sedimentation rate level as a predictor of the presence of osteomyelitis in diabetic foot infections. The erythrocyte sedimentation rate was found to be significantly higher in the presence of underlying bone infections. The optimal cutoff value was determined to be 70 mm/h with the highest positive and negative predictive value. Therefore, it can be assumed that a sedimentation rate of greater than 70 mm/h in a diabetic foot infection is strongly suspicious of osteomyelitis.

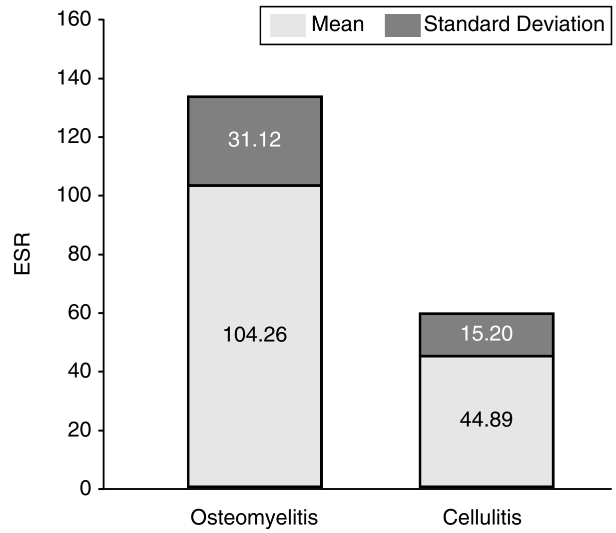

Figure 1. The mean and standard deviation of the erythrocyte sedimentation rate (ESR) for the two study groups.

While several studies have previously demonstrated elevations in erythrocyte sedimentation rate in the presence of osteomyelitis, most have failed to evaluate this relationship critically or have not specifically studied its use in the diabetic population.[14-16] Several of these investigations demonstrated elevation in the sedimentation rate in diabetic foot wounds with underlying bone involvement.[7, 18] Although the average erythrocyte sedimentation rate values in these studies were lower than the value obtained in this study, both exceeded the cutoff of 70 mm/h.

The medical literature documents an elevated erythrocyte sedimentation rate in females and the elderly as well as those with elevated creatinine levels.[19-23] In the present study, there were no significant differences in the sedimentation rate demonstrated with

Table 4. Statistical Significance Among Variables Tested in Cellulitis and Osteomyelitis Groups

Variable	Osteomyelitis Mean ± SD	Cellulitis Mean ± SD	*P* Value[a]
Age	58.8 ± 11.03	68.0 ± 16.51	0.126
Hb	10.8 ± 1.95	11.8 ± 1.48	0.151
Hct	32.9 ± 5.51	36.1 ± 4.06	0.126
Creatinine	1.3 ± 0.60	1.4 ± 0.59	0.668
ESR	104.3 ± 31.12	43.4 ± 15.20	0.000[b]
Gender			0.470

[a] *P* value was generated from Mann-Whitney test.
[b] Correlation is significant at $P = .05$.
Abbreviations: ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit.

Table 5. Sensitivity and Specificity of Erythrocyte Sedimentation Rate in Indicating Osteomyelitis

Cutoff Value (mm/h)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
≥ 60	89.5	90.0	94.4	81.8
≥ 65	89.5	90.0	94.4	81.8
≥ 70	89.5	100.0	100.0	83.3
≥ 75	84.2	100.0	100.0	79.6
≥ 80	78.9	100.0	100.0	71.4

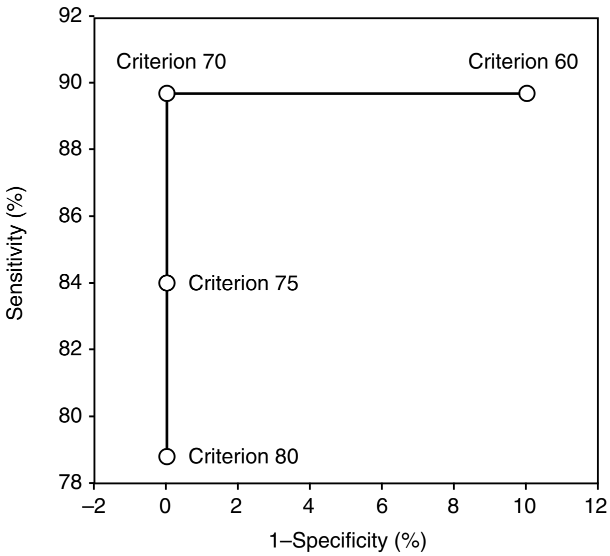

Figure 2. The ROC curve obtained to determine the cutoff level for the erythrocyte sedimentation rate that maximized the sensitivity without compromising the specificity in indicating the presence of osteomyelitis.

respect to the patients' age, gender, or creatinine levels. The authors did, however, demonstrate a negative association between the sedimentation rate and both hemoglobin and hematocrit levels. Many authors have related an increase in erythrocyte sedimentation rate as hemoglobin and hematocrit levels decrease.[21, 23] Duration and type of diabetes were not evaluated as the literature has demonstrated that this does not affect fibrinogen levels, which are the most influential factor in determining erythrocyte sedimentation rate levels.[9, 24-27]

Limitations of this investigation include the small number of cases reviewed. In further investigations, a prospective evaluation in which all patients with osteomyelitis are confirmed with pathology would improve the value of this study. In addition, the authors did not correlate location of the bone involvement with laboratory values. It may prove that the presence of infection in highly vascular areas of the foot or body may affect the sedimentation rate. Although it has been stated to be inconsequential, it may prove beneficial to investigate the type and duration of diabetes mellitus in these patients, and more importantly, to investigate glycemic control.

Summary

The erythrocyte sedimentation rate offers the physician treating the diabetic foot a simple, inexpensive, and minimally invasive means of evaluation. It also offers further information to suggest the presence of bone involvement. In combination with clinical signs of infection, most cases of osteomyelitis can be identified without time-consuming and costly imaging modalities, such as MRI and bone scans. It is of paramount importance that these diabetic foot infections be treated in a timely manner to avoid further loss of limb and life. The authors have demonstrated a high predictive value in this study and feel that in conjunction with a thorough clinical examination, an elevated erythrocyte sedimentation rate may help the physician diagnose the presence of osteomyelitis with confidence, thus allowing expedient treatment and higher rates of limb salvage.

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