# The ALT-70 cellulitis model maintains predictive value at 24 and 48 hours after presentation

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***Background:*** Cellulitis has many potential mimickers, and its misdiagnosis often leads to unnecessary hospitalizations and higher health care costs. The ALT-70 predictive model offers an objective tool to help differentiate between cellulitis and other clinically similar conditions at the time of initial emergency department (ED) presentation.

***Objective:*** To evaluate the performance of the ALT-70 predictive model at 24 and 48 hours following ED presentation.

***Methods:*** We performed a retrospective review of our prior cohort and expanded our data collection to include data at 24 and 48 hours after initial ED presentation. We compared classification measures for the ALT-70 at the time of initial ED presentation, 24 hours after presentation, and 48 hours after presentation.

***Results:*** There was a statistically significant difference in median ALT-70 score between patients with true cellulitis and those with mimickers of cellulitis at all time points. Sensitivity, specificity, positive predictive value, and negative predictive value of the ALT-70 score was similar across all 3 time points.

***Limitations:*** Single-center design may reduce generalizability.

***Conclusion:*** At 24 and 48 hours, the ALT-70 performed similarly to the way it performed at the time of initial ED presentation, allowing for its use in a wider array of clinical settings. (J Am Acad Dermatol 2019;81:1252-6.)

***Key words:*** ALT-70; cellulitis; lower extremity cellulitis; misdiagnosis; skin and soft-tissue infection; SSTI.

Cellulitis is a common skin and soft-tissue infection that results in an estimated 2.9 million emergency department (ED) visits annually, with the lower extremities being the most common anatomic region affected. In 2013, patient visits associated with a coded diagnosis of cellulitis were estimated to have resulted in ED and inpatient service charges of $4.2 billion and $9.5 billion, respectively.[1] Additionally, between 14% and 17% of patients seen in the ED with cellulitis are admitted, accounting for 10% of all infectious disease–related hospitalizations each year.[2-4]

Cellulitis is often misdiagnosed given the large number of conditions that have similar clinical

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features. These cellulitis mimickers are often termed *pseudocellulitis* and most commonly include vascular causes (eg, venous stasis dermatitis, deep vein thrombosis), noninfectious inflammatory disorders (eg, contact dermatitis, gout), and other infectious causes (eg, ecthyma gangrenosum, tinea pedis).[5]

The similar appearance of pseudocellulitis and cellulitis can often lead to misdiagnoses at a rate ranging from 30% to 90%, resulting in unnecessary cost to both patients and the health care system. Misdiagnosis of cellulitis may lead to between 50,000 and 130,000 unnecessary hospitalizations and $195 to $515 million in health care spending per year.[5,6] High misdiagnosis rates are further attributed to the current absence of a criterion standard diagnostic tool for cellulitis.[7]

**CAPSULE SUMMARY**

- The ALT-70 is a prospectively validated tool to assist in differentiating between cellulitis and pseudocellulitis at the time of initial ED presentation.
- We have retrospectively shown that the performance of the ALT-70 at 24 and 48 hours after initial ED presentation is similar to its performance at the time of initial ED presentation.

We previously published the ALT-70 cellulitis predictive model, a clinical decision support tool that incorporates objective clinical and laboratory measures to distinguish between lower extremity cellulitis and pseudocellulitis.[8] Its performance has been replicated in a prospective cohort study.[9] As the ALT-70 predictive model was intended to be used at the time of initial ED presentation, there has been no assessment of this model at later time points. Given the high rate of admissions for patients with presumed cellulitis, the ability to evaluate and re-evaluate patients with presumed cellulitis at time points later than their initial presentation is of significant value to clinicians who manage these patients after they have been admitted to the hospital.[2,3] In an effort to expand on the range of time points at which this model can be used, we sought to evaluate the predictive value of the ALT-70 model at 24 and 48 hours after initial ED presentation.

## METHODS

### Chart review and data collection

We performed a retrospective chart review of patients presenting to and admitted through the ED of a large urban hospital between June 2010 and December 2012 that were diagnosed with lower extremity cellulitis. This was the same cohort of patients used in initial development of the ALT-70, as previously reported.[8] The patients who were eligible for inclusion in the study were those whose condition was given a primary diagnosis of cellulitis by either the ED or admitting teams, presented directly to the ED, and were admitted following the diagnosis. Patients with any of the following were excluded from the study: cellulitis not located on the lower extremities; intravenous antibiotic use within 48 hours before ED visit; penetrating trauma, abscess, burn, or a known history of osteomyelitis, diabetic ulcer, surgery within past 30 days; and indwelling hardware at the site of infection.[8]

Each patient chart was reviewed systematically to record patient presentation to the ED and hospital course. Variables collected at the time of presentation included patient age, heart rate, findings of a physical examination of the lesion to assess for symmetry, and white blood cell count. In addition, heart rate and white blood cell count were recorded both 24 and 48 hours after initial ED presentation. The white blood cell count recorded was the first of the morning on the given day, and each patient's daily maximum heart rate was recorded. Patients were determined to be tachycardic at 24 and 48 hours after presentation to the ED if their maximum heart rate was greater than 90 beats per minute for that day. If the patient was discharged sooner than 48 hours following initial presentation, heart rate and white blood cell count were recorded only up until the day of discharge.

ALT-70 score was calculated at the time of initial ED presentation, 24 hours after the initial presentation, and 48 hours after the initial presentation. This model has been previously evaluated in lower extremity cellulitis and assigns points to 4 objective variables collected at the time of ED presentation (Table I). Recommendations based on this model were stratified by outcome: 0 to 2 points favored pseudocellulitis, 3 to 4 points indicated that the patient might benefit from inpatient dermatology consultation, and 5 or more points represented a likely cellulitis.[8]

In this analysis, patient age and rash symmetry recorded on physical examination at the time of ED presentation were used for calculation of ALT-70 score across all time points, whereas heart rate and white blood cell count were recorded each day. ALT-70 scores were calculated for patients on the basis of the presence of these criteria, as detailed previously.

*Abbreviations used:*

CI: confidence interval
ED: emergency department
PPV: positive predictive value

### Statistical analysis

We calculated classification measures, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value for the ALT-70 predictive model at the following time points: (1) time of presentation in the ED, (2) 24 hours following ED presentation, and (3) 48 hours following ED presentation. These scores were calculated with ALT-70 score cutoffs of both 3 and 5. In addition, receiver operating characteristic curves for the model at each of the 3 time points were constructed as a continuous predictor of cellulitis. Analyses were performed by using SAS software (version 9.4, SAS Inc, Cary, NC).

## RESULTS

### Patient demographics and clinical characteristics

In our initial investigation, we identified a total of 840 patients with presumed cellulitis, 259 of whom met the inclusion criteria for our study.[8] At 24 hours after initial presentation, 228 of these patients remained in the hospital; at 48 hours, the number of patients remaining in the hospital decreased to 209 patients. Of the 259 patients at initial presentation, 79 (30.5%) were given an alternate diagnosis during their hospitalizations or within 30 days of discharge and classified as pseudocellulitis, whereas 180 (69.5%) were discharged with a diagnosis of cellulitis (Table I).

At the time of ED presentation, 28 patients in the pseudocellulitis group (35.4%) had bilateral lower extremity involvement at presentation versus 13 (7.2%) in the cellulitis group ($P < .001$). White blood cell count at the time of ED presentation showed a total of 117 patients with leukocytosis (white blood cell count >10,000/uL): 25 patients (31.6%) in the pseudocellulitis group and 92 patients (51.1%) in the cellulitis group ($P = .004$). At 24 and 48 hours after ED presentation, there was no statistically significant difference between the pseudocellulitis and cellulitis groups for leukocytosis and tachycardia individually.

### Predictive value of ALT-70 score at various time points

ALT-70 score at the time of ED presentation was higher for patients with cellulitis (median, 5; interquartile range, 3-5) than for patients with pseudocellulitis (median, 3; interquartile range, 2-4) ($P < .001$) The median ALT-70 score for patients with cellulitis was similarly higher at both at 24 hours ($P < .001$) and 48 hours ($P < .001$) after ED presentation. The predictive value of the ALT-70 at 24 and 48 hours was similar to that at the time of initial presentation, as evidenced by similar PPVs across all time points for an ALT-70 score greater than 5 (Table II). An ALT-70 score greater than 5 conferred the highest PPV for lower extremity cellulitis at time 48 hours following admission (84.9%). The negative predictive value of the ALT-70 was consistent across all time points for their respective cutoff values (Table III).

Receiver operating characteristic curves were constructed for ALT-70 score at each of the 3 time points. Although ALT-70 score at the time of ED presentation showed the highest accuracy (C-statistic, 0.74; 95% confidence interval [CI], 0.68-0.81), the ALT-70 scores at 24 hours (C-statistic, 0.70; 95% CI, 0.63-0.77) and 48 hours (C-statistic: 0.71; 95% CI, 0.63-0.78) had good model performance in discriminating lower extremity cellulitis (Fig 1).

**Table I.** Calculation of ALT-70 score

| Criterion | Definition | Score |
|---|---|---|
| Asymmetry | Unilateral lower extremity involvement | +3 |
| Leukocytosis | White blood cell count in ED $\geq 10{,}000/\mu L$ | +1 |
| Tachycardia | Heart rate in ED $\geq 90$ bpm | +1 |
| Age | $\geq 70$ y | +2 |

*ED,* Emergency department.

## DISCUSSION

Our study builds on our previous work demonstrating the predictive value of the ALT-70 score at the time of initial presentation to the ED by expanding the range of time at which this model can be applied. We have shown that the model holds strong predictive value at the time of ED presentation (C-statistic, 0.74), 24 hours after presentation (C-statistic, 0.70), and 48 hours after presentation (C-statistic, 0.71).

Importantly, the high PPV of the ALT-70 with a cutoff score of 5 (82.2%-84.9%), particularly at 48 hours (84.9%), allows clinicians to be confident in their decision to initiate or continue treatment with empiric antibiotics. Further, the high sensitivity of the ALT-70 with a cutoff score of 3 at all time points (94.4%-96.5%) allows clinicians to be similarly confident that a patient with an ALT-70 score between 0 and 2 within the first 48 hours of presentation is

**Table II.** Patient demographics and clinical characteristics

| Characteristic | Overall | Pseudocellulitis | Cellulitis | *P* value |
|---|---|---|---|---|
| ALT-70 in ED | | | | |
| Patients, n | 259 | 79 | 180 | |
| Age ≥70 y, n (%) | 98 (37.8) | 24 (30.4) | 74 (41.1) | .10 |
| Bilateral lesions, n (%) | 41 (15.8) | 28 (35.4) | 13 (7.2) | <.001 |
| WBC >10,000/uL, n (%) | 117 (45.2) | 25 (31.6) | 92 (51.1) | .004 |
| HR >90 bpm, n (%) | 120 (46.3) | 31 (39.2) | 89 (49.4) | .13 |
| Median ALT-70 score (IQR) | 4 (3-5) | 3 (2-5) | 5 (4-5) | <.001 |
| ALT-70 at 24 h | | | | |
| Patients, n | 228 | 70 | 158 | |
| WBC >10,000/uL, n (%) | 80 (35.1) | 19 (27.1) | 61 (38.6) | .094 |
| HR >90 bpm, n (%) | 89 (39.0) | 29 (41.4) | 60 (38.0) | .62 |
| Median ALT-70 score (IQR) | 4 (3-5) | 3 (2-5) | 5 (3-5) | <.001 |
| ALT-70 at 48 h | | | | |
| Patients, n | 209 | 66 | 143 | |
| WBC >10,000/uL, n (%) | 61 (29.2) | 15 (22.7) | 46 (32.2) | .16 |
| HR >90 bpm, n (%) | 73 (34.9) | 22 (33.3) | 51 (35.7) | .74 |
| Median ALT-70 score (IQR) | 4 (3-5) | 3 (2-4) | 5 (3-5) | <.001 |

*ED*, Emergency department; *HR*, heart rate; *IQR*, interquartile range; *WBC*, white blood count.

**Table III.** Sensitivity, specificity, positive predictive value, and negative predictive for the decision to treat

| Characteristic | Positive, n | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|
| ALT-70 score ≥3 points | | | | | |
| In ED | 223 | 96.5% | 29.1% | 74.9% | 79.3% |
| At 24 h | 203 | 95.6% | 25.7% | 74.4% | 72.0% |
| At 48 h | 182 | 94.4% | 28.8% | 74.2% | 70.4% |
| ALT-70 score ≥5 points | | | | | |
| In ED | 129 | 61.3% | 70.9% | 82.2% | 45.5% |
| At 24 h | 101 | 52.5% | 74.3% | 82.2% | 40.9% |
| At 48 h | 86 | 51.0% | 80.3% | 84.9% | 43.1% |

*ED*, Emergency department; *NPV*, negative predictive value; *PPV*, positive predictive value.

unlikely to have lower extremity cellulitis. Implementation of this tool may help decrease the high cost associated with misdiagnosis and reduce risks associated with unnecessary antibiotic exposure on both the individual patient and population levels.[4,10-13]

The ALT-70 predictive model offers a rapid, objective point-of-care tool that can be used by practitioners to differentiate between lower extremity cellulitis and its mimickers. Currently, there is no criterion standard laboratory test in the diagnosis of cellulitis, and until such an objective measure is available, we hope that clinical decision support with tools such as the ALT-70 may help guide clinicians. Formal dermatology consultation has also been shown to increase diagnostic accuracy of cellulitis and may provide additional benefit in conjunction with use of the ALT-70 tool, particularly when the ALT-70 score falls in the intermediate range of 3 to 4.[6,14]

### Limitations

Our findings must be interpreted in the context of our study design. Our study was performed retrospectively on patients admitted through the ED of a single institution, and as such, additional studies are needed to assess the generalizability of our results. Also, our study design allowed for the final diagnosis of cellulitis to be made by nondermatologists, who are often less familiar with etiologies of pseudocellulitis, which could lead to overdiagnosis of cellulitis. Our cohort was identified by using strict inclusion and exclusion criteria, which limits the application of our model until further studies are completed. Prospective validation is necessary.

## CONCLUSION

In this study, we have demonstrated that the accuracy of the ALT-70 tool for evaluation of lower extremity cellulitis can be expanded to inpatients at 24 and 48 hours after ED presentation. The ALT-70

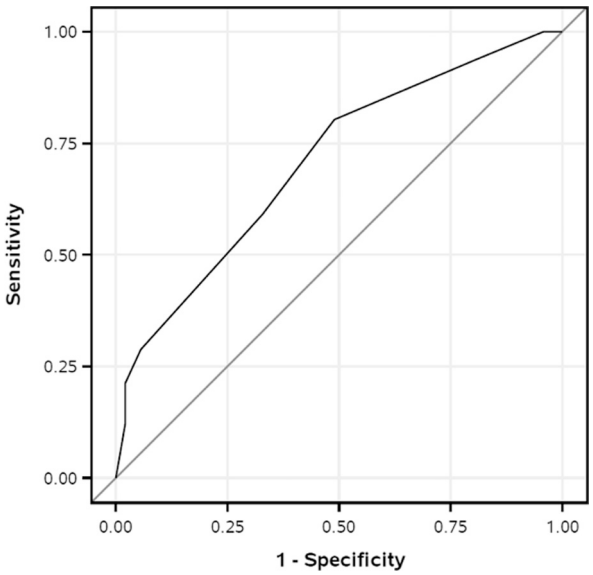


**Fig 1.** Receiver operating characteristic curve for ALT-70 score at 48 hours. C-statistic .707 (95% confidence interval, 0.633-0.781).

predictive model is a point-of-care tool that can help reduce the misdiagnosis of cellulitis and subsequent treatment that leads to significant cost to both patients and the health care system. By effectively expanding the range of times at which this tool can be used, we can increase its usefulness and expand its use to inpatient settings.

## REFERENCES

1. Li DG, Joyce C, Mostaghimi A. Patient factors associated with nationwide emergency department utilization for cellulitis. *Am J Emerg Med*. 2019;37(2):361-363.
2. Khachatryan A, Patel D, Stephens J, Johnson K, Patel A, Talan D. Skin and skin structure infections (SSSIs) in the emergency department (ED): who gets admitted. Poster Presentation at the Society for Academic Emergency Medicine (SAEM) 2014, May 13 -17, 2014, Dallas, Texas.
3. Talan DA, Salhi BA, Moran GJ, et al. Factors associated with decision to hospitalize emergency department patients with skin and soft tissue infection. *West J Emerg Med*. 2015;16(1):89.
4. Christensen KLY, Holman RC, Steiner CA, Sejvar JJ, Stoll BJ, Schonberger LB. Infectious disease hospitalizations in the United States. *Clin Infect Dis*. 2009;49(7):1025-1035.
5. Weng Q, Raff AB, Cohen JM, et al. Costs and consequences associated with misdiagnosed lower extremity cellulitis. *JAMA Dermatol*. 2017;153(2):141-146.
6. Li DG, Di Xia F, Khosravi H, et al. Outcomes of early dermatology consultation for inpatients diagnosed with cellulitis. *JAMA Dermatol*. 2018;154(5):537-543.
7. Pallin DJ, Bry L, Dwyer RC, et al. Toward an objective diagnostic test for bacterial cellulitis. *PLoS One*. 2016;11(9):e0162947.
8. Raff AB, Weng QY, Cohen JM, et al. A predictive model for diagnosis of lower extremity cellulitis: a cross-sectional study. *J Am Acad Dermatol*. 2017;76(4):618-625.
9. Li DG, Dewan AK, Di Xia F, Khosravi H, Joyce C, Mostaghimi A. The ALT-70 predictive model outperforms thermal imaging for the diagnosis of lower extremity cellulitis: a prospective evaluation. *J Am Acad Dermatol*. 2018;79(6):1076-1080.
10. Kroshinsky D, Grossman ME, Fox LP. Approach to the patient with presumed cellulitis. *Semin Cutan Med Surg*. 2007;26(3):168-178.
11. World Health Organization. *Report on the Burden of Endemic Health Care-Associated Infection Worldwide*. Geneva, Switzerland: World Health Organization; 2011.
12. World Health Organization. *Antimicrobial Resistance: Global Report on Surveillance*. Geneva, Switzerland: World Health Organization; 2014.
13. US Department of Health and Human Services. Centers for Disease Control and Prevention. *Antibiotic Resistance Threats in the United States, 2013*. Atlanta, GA: Centers for Disease Control and Prevention; 2013.
14. Strazzula L, Cotliar J, Fox LP, et al. Inpatient dermatology consultation aids diagnosis of cellulitis among hospitalized patients: a multi-institutional analysis. *J Am Acad Dermatol*. 2015;73(1):70-75.