



What Is the Accuracy of Physical Examination, Imaging, and the LRINEC Score for the Diagnosis of Necrotizing Soft Tissue Infection?

TAKE-HOME MESSAGE

Computed tomography (CT) has superior sensitivity compared with radiography for the diagnosis of necrotizing soft tissue infection, although different imaging findings have various diagnostic test characteristics. No single element of the physical examination, radiography, or the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has sufficient sensitivity to exclude necrotizing soft tissue infection.

METHODS

DATA SOURCES

Authors searched MEDLINE, PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Database of Systematic Reviews from inception through November 13, 2017. Search terms included “necrotizing fasciitis,” “necrotizing skin and soft tissue infection,” “necrotizing soft tissue infection,” “gas gangrene,” and “Fournier’s gangrene.”

STUDY SELECTION

The authors included all English-language abstracts and full-text articles. Studies included retrospective and prospective observational studies, randomized controlled trials, and quasi-randomized controlled trials of adults (≥ 16 years) with suspected necrotizing soft tissue infection in an emergency department (ED), hospital ward, or ICU setting. Included studies evaluated the test characteristics of one or more of

EBEM Commentators

Michael D. April, MD, DPhil

Brit Long, MD

Department of Emergency Medicine

San Antonio Uniformed Services Health

Education Consortium

Fort Sam, Houston, TX

Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.

Editor’s Note: This is a clinical synopsis, a regular feature of the *Annals’* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is:

Fernando SM, Tran A, Cheng W, et al. Necrotizing soft tissue infection: diagnostic accuracy of physical examination, imaging, and LRINEC score: a systematic review and meta-analysis. *Ann Surg.* 2018; <https://doi.org/10.1097/SLA.0000000000002774>.

Results

Meta-analytic estimates for diagnostic accuracy of physical examination features, imaging, and LRINEC score for necrotizing soft tissue infection.

Variable	No. of Studies (No. of Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %	Positive LR (95% CI)	Negative LR (95% CI)
Physical examination					
Fever	4 (647)	46.0 (38.9–53.2)	77.0 (59.7–88.1)	1.98 (1.12–3.51)	0.70 (0.59–0.84)
Hemorrhagic bullae	5 (951)	25.2 (12.8–43.7)	95.8 (87.3–98.7)	5.97 (2.89–12.32)	0.78 (0.66–0.93)
Hypotension	6 (1,014)	21.0 (9.4–40.4)	97.7 (91.4–99.4)	9.20 (3.87–21.86)	0.81 (0.68–0.96)
Imaging					
Radiography	4 (478)	48.9 (24.9–73.4)	94.0 (63.8–99.3)	8.17 (1.61–41.47)	0.54 (0.36–0.82)
CT (fascial gas only)	7 (787)	88.5 (55.5–97.9)	93.3 (80.8–97.9)	13.27 (4.24–41.50)	0.12 (0.03–0.62)
CT (fascial edema or enhancement or gas)	6 (700)	94.3 (81.2–98.5)	76.6 (21.3–97.5)	4.04 (0.062–26.47)	0.07 (0.02–0.24)

the following: physical examination, imaging modalities, or LRINEC score for the diagnosis of necrotizing soft tissue infection. Necrotizing soft tissue infection was confirmed by operative findings, histopathologic tissue examination, or death from suspected necrotizing soft tissue infection. Two authors independently evaluated the title and abstract of each study, followed by the full-text review for potentially eligible articles. These authors resolved all discrepancies in regard to study eligibility through mutual agreement.

DATA EXTRACTION AND SYNTHESIS

Two authors independently used a predesigned data extraction tool to collect all diagnostic accuracy data. Two authors independently assessed the risk of bias for each study, using the Quality Assessment of Diagnostic Accuracy Studies tool.¹ They pooled results by applying the hierarchic summary receiver operating characteristic model² and calculated summary point estimates of measures of diagnostic accuracy. Authors assessed heterogeneity through the scatter plot surrounding the summary receiver operating characteristic and the confidence or prediction regions of the summary point, in addition to forest plots.

Continued.

Variable	No. of Studies (No. of Patients)	Sensitivity (95% CI), %	Specificity (95% CI), %	Positive LR (95% CI)	Negative LR (95% CI)
LRINEC score					
≥6	14 (4,339)	68.2 (51.4–81.3)	84.8 (75.8–90.9)	4.49 (2.74–7.35)	0.38 (0.24–0.60)
≥8	9 (1,905)	40.8 (28.6–54.2)	94.9 (89.4–97.6)	7.94 (3.44–18.32)	0.62 (0.50–0.78)

CI, Confidence interval; LR, likelihood ratio.

Of 2,290 initial citations, the authors included 23 studies including 16 retrospective cohort studies, 2 prospective cohort studies, and 5 retrospective case-control studies. Pooled sensitivity values for physical examination findings ranged from 21.0% for hypotension to 46.0% for fever (Table). The sensitivity of CT presence of fascial edema, fascial enhancement, or fascial gas was significantly higher than the sensitivity of radiography (94.3% versus 48.9%). Finally, the sensitivity of LRINEC scores was poor, although the specificity for scores greater than or equal to 8 was very good (94.9%). Of the included studies, 11 (47.9%) had unclear risk of bias and 10 (43.5%) had potential for high risk of bias in the use of the index test (physical examination, imaging, or LRINEC score). Sensitivity analyses excluding these latter 10 studies yielded sensitivity and specificity estimates comparable to the base-case estimates.

Commentary

Necrotizing soft tissue infection is a rapidly progressive disease associated with significant morbidity and mortality.³ Patient survival demands rapid diagnosis,

expeditious initiation of broad-spectrum antibiotics, and surgical debridement.⁴ The reference standard for the diagnosis of necrotizing soft tissue infection is physical findings during surgical exploration in the operating room.³ Given an inability to obtain this reference standard, emergency physicians must rely on other tools to prompt surgical consultation to ultimately make the diagnosis. This diagnosis can be notoriously elusive in the ED, given that it can mimic far more common yet less nefarious disease processes such as cellulitis.⁵ Hence, it is imperative that emergency physicians be facile with the diagnostic accuracy of tests commonly used to identify necrotizing soft tissue infection.

This meta-analysis highlighted the reality that many of the tools at the disposal of the emergency physician to identify necrotizing soft tissue infection have limited utility. In particular, physical examination findings and radiography have poor sensitivity for necrotizing soft tissue infection. Similarly, although the LRINEC score showed promise for diagnostic accuracy in its initial derivation and validation cohorts,⁶ the present meta-analysis

demonstrated that its sensitivity was inadequate to reliably exclude the diagnosis. Of the tools studied by this meta-analysis, only CT imaging demonstrated robust sensitivity for necrotizing soft tissue infection, although this modality can also miss the diagnosis. This meta-analysis further highlighted the potential pitfalls of considering CT imaging results as strictly binary (ie, positive versus negative). In fact, imaging results are comparable to physical examination and laboratory study results in that they may encompass various findings, each of which have distinct diagnostic utility.

Limitations of this meta-analysis included study quality. Study quality limitations related to the lack of detail provided by many of the studies in regard to whether individuals conducting the diagnostic tests were blinded to the final diagnosis. Furthermore, 5 included studies were retrospective case-control studies at potential risk of recall bias, and there were no randomized controlled studies. Another limitation of this meta-analysis is clinical heterogeneity across included studies, arising from significant variations in inclusion criteria. Three studies evaluated cervical necrotizing soft tissue

infection, and no studies evaluated diagnostic accuracy stratified by infected body site. This is potentially problematic because the accuracy of different diagnostic tools may differ according to body site, much as body site significantly affects necrotizing soft tissue infection prognosis.⁷ Finally, the authors did not evaluate the diagnostic accuracy of other important tests such as ultrasonography or individual components of the LRINEC score.

This meta-analysis supports previous recommendations, such as those by the Infectious Diseases Society of America, stating that clinicians should use clinical judgment to make this challenging diagnosis and that individual physical examination elements and radiographs alone are insufficient to exclude the diagnosis.⁸ Further study is necessary to evaluate the use of ultrasonography and examine test characteristics for subtypes of necrotizing soft tissue infection. The literature would also benefit from examination of alternative combinations of tests and physical examination findings to potentially develop clinical scoring systems with diagnostic accuracy for necrotizing soft tissue infection that are superior to the LRINEC score.

The views expressed herein are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force and Department of Defense, or the US government.

1. Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol.* 2003;3:25.
2. Rutter CM, Gatsonis CA. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Stat Med.* 2001;20:2865-2884.
3. Stevens DL, Bryant AE. Necrotizing soft-tissue infections. *N Engl J Med.* 2017;377:2253-2265.
4. Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. *Clin Infect Dis.* 2007;44:705-710.
5. Henry SM, Davis KA, Morrison JJ, et al. Can necrotizing soft tissue infection be reliably diagnosed in the emergency department? *Trauma Surg Acute Care Open.* 2018;3:e000157.
6. Wong CH, Khin LW, Heng KS, et al. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med.* 2004;32:1535-1541.
7. McHenry CR, Piotrowski JJ, Petrinic D, et al. Determinants of mortality for necrotizing soft-tissue infections. *Ann Surg.* 1995;221:558-563.
8. Stevens DL, Bisno AL, Chambers HF, et al; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2014;59:e10-e52.