INFECTIOUS DISEASE/SYSTEMATIC REVIEW SNAPSHOT

TAKE-HOME MESSAGE

In teens and young adults (<26 years) with sore throat, the likelihood of mononucleosis is increased with lymphadenopathy (posterior cervical, axillary, or inguinal), palatine petechiae, splenomegaly, and atypical lymphocytosis.

METHODS

DATA SOURCES

The authors searched PubMed (1966 to 2016) and EMBASE (1947 to 2015) for studies that reported diagnostic accuracy with the search terms "mononucleosis" AND "specificity or predictive value or likelihood ratio or sensitivity or accuracy." In addition, they searched the reference lists of identified articles, as well as Google Scholar.

STUDY SELECTION

The review included diagnostic studies with abstracts conducted with patients who were consecutively enrolled or a convenience sample with sore throat or mononucleosis; provided diagnostic accuracy data for the medical history, physical examination, or WBC count; and reported sufficient data to calculate sensitivity, specificity, or likelihood ratios (LRs). The authors also included studies comparing index test with reference standard, defined as the Epstein-Barre virus viral capsid antigen immunoglobulin M test or a heterophile antibody test. They excluded studies with hospitalized patients and those deemed to have incorporation bias.

DATA EXTRACTION AND SYNTHESIS

Two authors independently extracted data, and disagreements were resolved by consensus. Study

What Elements Suggest Infectious Mononucleosis?

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Results

Accuracy of clinical findings for the diagnosis of mononucleosis.

Clinical Finding	Number of Studies*	Sensitivity (95% CI)	Specificity (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Palatine petechiae	1,1	0.25–0.27	0.95 (0.93–0.97)	5.3 (2.1–13.0)	1.0 (0.6–1.0)
Posterior cervical lymphadenopathy	2,1	0.64 (0.40–0.83)	0.87 (0.84–0.89)	3.1 (1.6–5.9)	0.69 (0.46–1.00)
Inguinal or axillary lymphadenopathy, or both	2,1	0.23 (0.08–0.51)	0.82–0.91	3.0–3.0	0.57–0.81
Splenomegaly	2,2	0.26 (0.11–0.49)	0.71–0.99	1.9–6.6	0.65–0.94
Atypical lymphocytes ≥10%	0,3	0.66 (0.52–0.78)	0.92 (0.71–0.98)	11 (2.7–35.0)	0.37 (0.26–0.51)

CI, Confidence interval.
*Number of studies with data to calculate sensitivity and specificity. If there were only data from a single study, the point estimate and a 95% CI were presented. If there were 2 studies, ranges were presented. For 3 studies, univariate meta-analysis data were presented.

Authors screened 670 abstracts and selected 117 for full-text review, of which 11 met inclusion criteria. A total of 4,769 patients were included, of whom 2,345 had serologically confirmed mononucleosis. Three studies were prospective cohort studies, 3 were retrospective laboratory studies without clinical information, and 5 were case series with confirmed mononucleosis. Of the studied elements, atypical lymphocytes had the greatest positive LR (Table). None of the examined elements were sufficient to exclude the diagnosis.

Commentary

Infectious mononucleosis is a disease of primarily teenagers and young adults, occurring in approximately 7% with sore throat.[3] Although it is a viral illness, making the diagnosis of mononucleosis is important because it allows clinicians to guide symptomatic treatment while avoiding unnecessary antibiotics, educate patients on limiting physical activities because of the risk of splenic injury in the setting of splenomegaly, and offer a realistic prognosis because

Systematic Review Snapshot

quality was assessed with *Rational Clinical Examination* quality levels.[1] Risk of bias was determined with the Quality Assessment of Diagnostic Accuracy Studies criteria.[2] Meta-analysis of clinical findings was summarized with univariate and bivariate random-effects models. Heterogeneity for LRs was calculated with the I^2 statistic.

symptoms may last for several weeks.

Determining who has mononucleosis can be challenging because symptoms of sore throat and malaise are nonspecific. This review, although limited by the quality and age of the studies, offers clinicians useful guidance. The presence of lymphadenopathy (posterior cervical, axillary, and inguinal), palatine petechiae, splenomegaly, and atypical lymphocytosis significantly increases the likelihood of mononucleosis, whereas the absence of any lymphadenopathy reduces the likelihood. The authors advocate the use of the WBC count as an adjunct to clinical signs and symptoms, especially early in the disease process because the false-negative rate for the antibody test can be approximately 25%.[4] The presence of a sore throat and a WBC count with greater than 50% lymphocytosis and greater than 10% atypical lymphocytes in a teen or young adult patient increases the likelihood of mononucleosis, with a positive predictive value of 73%.

In summary, emergency clinicians who are considering the diagnosis of mononucleosis should look for lymphadenopathy (posterior cervical, axillary, and inguinal), palatine petechiae, splenomegaly, and atypical lymphocytosis to improve diagnostic accuracy and guide appropriate management.

1. Simel DL. JAMA evidence: a primer on the precision and accuracy of the clinical examination: update. In: Simel DL, Rennie D, eds. *The Rational Clinical Examination*. New York, NY: McGraw-Hill; 2009.
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3. Del Mar C, Pincus D. Incidence patterns of respiratory illness in Queensland estimated from sentinel general practice. *Aust Fam Physician*. 1995;24:625-632.
4. Elgh F, Linderholm M. Evaluation of six commercially available kits using purified heterophile antigen for the rapid diagnosis of infectious mononucleosis compared with Epstein-Barr virus-specific serology. *Clin Diagn Virol*. 1996;7:17-21.

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