What Is The Diagnostic Accuracy of Rapid Nucleic Acid Tests for Group A Streptococcal Pharyngitis?

TAKE-HOME MESSAGE

Rapid nucleic acid tests are more sensitive and equally specific compared with rapid antigen detection tests for detecting group A streptococcal pharyngitis.

METHODS

DATA SOURCES

The authors searched MEDLINE, Embase, and Web of Science articles published from January 1, 1990, to November 4, 2020. The authors also searched references of included studies, Google Scholar, online resources of professional societies, and conference abstracts, and they sought unpublished data.

STUDY SELECTION

Cross-sectional studies and randomized trials reporting the diagnostic accuracy of rapid nucleic acid tests for diagnosing group A streptococcus using a throat culture on simple blood agar incubated for 48 hours as a reference standard were included. Commercial rapid nucleic acid test results had to be available within 2 hours of being performed. No language, age, or clinical setting restrictions were applied. Studies prior to 1990 were not included because rapid nucleic acid tests were not available prior to that time.

DATA EXTRACTION AND SYNTHESIS

Two authors independently evaluated the studies for inclusion and exclusion, and discrepancies

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals*' Systematic Review Snapshot series. The source for this systematic review snapshot is as follows: **Dubois C, Smeesters PR, Refes Y, et al. Diagnostic accuracy of rapid nucleic acid tests for group A streptococcal pharyngitis: systematic review and meta-analysis. *Clin Microbiol Infect.* 2021;27:1736-1745.**

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

Results

Table. Test characteristics of rapid nucleic acid test and rapid antigen detection test for group A streptococcus.

Test	Sensitivity (95% CI)	Specificity (95% CI)	+LR (95% CI)	−LR (95% CI)
RNAT	97.5% (96.2-98.3)	95.1% (93.6-96.3)	20.0 (15.2-26.4)	0.03 (0.02-0.04)
RNAT vs RADT*	96.8% (94.6-98.1) vs 82.3% (65.0-92.1)	97.0% (94.3-98.5) vs 97.2% (94.3-98.6)	32.4 (16.9-62.2) vs 26.4 (12.9-54.2)	0.03 (0.02-0.06) vs 0.18 (0.08-0.39)

CI, Confidence interval; *LR*, likelihood ratio; *RNAT*, rapid nucleic acid test; *RADT*, rapid antigen detection test.
*Direct comparison.

A total of 38 cross-sectional studies were included, with 17,411 test results. Group A streptococcus was present in 22% of the cases overall, with an estimated group A streptococcus prevalence of 27%. The majority (82%) of the studies were conducted in the United States using 12 different rapid nucleic acid test commercial kits. Fifteen studies included adults and children, 12 studies included only children, and 11 studies did not specify the patient population. Rapid nucleic acid tests were found to be highly sensitive and specific for group A streptococcus. Rapid nucleic acid tests were more

were resolved via discussion. If there were studies with potentially overlapping populations, only the most recent report was included. For each study included, the authors independently extracted the number of true positives, true negatives, false positives, and false negatives for each index test. When these were not directly reported, they were calculated from reported sensitivities and specificities. The authors assessed variability in accuracy across the studies using forest plots and receiver operating characteristic space, followed by meta-regression to evaluate variability and directly compare the accuracy of rapid nucleic acid test with that of rapid antigen detection test. The authors performed sensitivity analyses and evaluated bias using the Quality Assessment of Diagnostic Accuracy Studies-2 tool.

sensitive than rapid antigen detection tests in 13 direct comparison studies but demonstrated specificity similar to that of rapid antigen detection tests (Table). The risk of bias was high for flow and timing in 30 studies, patient selection in 7 studies, and index test in 5 studies. Applicability concerns about patient selection were high because only 5 of the 38 studies were conducted in an outpatient setting. However, there were fewer concerns about the index test and reference standard.

Commentary

Between 11 and 18 million Americans seek medical care for pharyngitis every year. Group A streptococcus is the causative agent in up to 15% of pharyngitis cases in adults and up to 35% of pharyngitis cases in children.[1] In the United States, approximately 1.5 per 1,000 patients develop complications, which include acute rheumatic fever, rheumatic heart disease, poststreptococcal glomerulonephritis, bacteremia, peritonsillar abscess, and retropharyngeal abscess.[2] Antibiotics, in addition to antipyretics and analgesics, may prevent suppurative complications and the nonsuppurative complication rheumatic fever (but not poststreptococcal glomerulonephritis) and, thus, shorten the duration of illness and decrease the risk of contagion 24 hours after treatment.[3] Appropriate diagnosis is an important component of care for a patient with group A streptococcus pharyngitis. Decreasing overtreatment with antibiotics in cases of viral pharyngitis is also imperative, given that 50% to 80% of all pharyngitis cases are viral.[4-6] Several tools are available to assist in determining the need for further evaluation and testing, including Centor and McIsaac scores.[7,8] A Centor score of 0 or a McIsaac score of ≤ 0 can likely result in the exclusion of group A streptococcus pharyngitis, but patients with a Centor score of >0 or a McIsaac score of ≥ 0 likely require further evaluation for group A streptococcus pharyngitis.[9] The gold standard for diagnosis is a throat culture, but this test is not typically available in an emergency department (ED) setting. Thus, an accurate point-of-care diagnostic test is critical for achieving balance between the appropriate diagnosis and treatment of group A streptococcus pharyngitis while improving antimicrobial stewardship.

This meta-analysis by Dubois et al[10] found that rapid nucleic acid tests were highly accurate for the diagnosis of group A streptococcus pharyngitis, with higher sensitivity and similar specificity compared with rapid antigen detection tests. However, there are several important limitations. First, only 3 of the 38 studies evaluated point-of-care testing by an untrained personnel versus those in a laboratory by a certified personnel, thus raising the question of the clinical applicability of the results in a point-of-care setting. Second, only 5 studies were performed in the ED setting, with majority conducted in a walk-in clinic or not reported, again raising concerns about applicability. Third, incomplete reporting prevented a complete subgroup analysis and meta-regression. Most studies did not describe the use of a clinical score, which may have led to selection bias and distortion of the diagnostic performance of rapid nucleic acid tests. The authors included single-strand DNA tests with lower sensitivity, which have been replaced by newer testing methods. However, a sensitivity analysis excluding this test found similar diagnostic capabilities of rapid nucleic acid tests. Finally, no study stated whether rapid nucleic acid test results impacted patient care.

Based on these data, rapid nucleic acid tests may be used as a stand-alone test for diagnosing group A streptococcus. However, further randomized data incorporating scoring systems and pretest probability in patients of all ages and evaluating rapid nucleic acid test impact on patient-centered outcomes are required in the ED setting. Clinicians using rapid nucleic acid tests should also consider clinical needs, available resources, and local epidemiology.

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