Interpreting SARS-CoV-2 Test Results

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A 53-year-old woman was referred to the gastroenterology clinic for endoscopy because of a submucosal gastric nodule. She had not received a COVID-19 vaccination and lived in Maryland, which had a 7-day cumulative COVID-19 case rate of 70 per 100,000 individuals at the time of her visit. Review of systems was unremarkable except for intermittent abdominal pain. She had no fever, cough, shortness of breath, difficulty breathing, muscle aches, headache, sore throat, anosmia, dysgeusia, or diarrhea. SARS-CoV-2 reverse transcriptase–polymerase chain reaction (RT-PCR) testing prior to the procedure was performed, in accordance with the American Society of Anesthesiologists Statement on Perioperative Testing1 for monitored anesthesia. Results of preoperative testing are shown in Table 1.

Based on the results, additional history was obtained. The patient reported testing positive for SARS-CoV-2 30 days prior at another hospital. At that time, she had symptoms of dry cough, low-grade fever, and body aches, which resolved after 14 days. Fourteen days before the current presentation, results of a rapid antigen test performed at a local pharmacy were negative for SARS-CoV-2.

Table 1. Patient’s Test Results

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Patient’s test result</th>
<th>Reference/standard range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count, ×10^3/μL</td>
<td>6.2</td>
<td>3.6-10.2</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>11.8</td>
<td>12.5-16.3</td>
</tr>
<tr>
<td>Platelet count, ×10^3/μL</td>
<td>384</td>
<td>152-348</td>
</tr>
<tr>
<td>SARS-CoV-2 reverse transcriptase-polymerase chain reaction</td>
<td>Detected</td>
<td>Not detected</td>
</tr>
</tbody>
</table>

Answer

C. Proceed with endoscopy, the patient is clinically recovered and not contagious

Test Characteristics

SARS-CoV-2 RT-PCR is the primary diagnostic test for COVID-19 (Medicare reimbursement, $75). The test amplifies targeted nucleic acid sequences to detect SARS-CoV-2 RNA. RT-PCR testing detects SARS-CoV-2 RNA at low levels, with analytic sensitivity of 98% and specificity of 97%.2 Analytic sensitivity and specificity refer to RT-PCR detection of SARS-CoV-2 RNA in laboratory samples, while clinical sensitivity and specificity refer to identifying patients with and without COVID-19. Clinical sensitivity is approximately 90% and clinical specificity is approximately 95%.3,4 Time from symptom onset, specimen source, and user error all affect clinical sensitivity (Table 2). Sensitivity of RT-PCR to detect patients with SARS-CoV-2 that can be cultured and infect others is 99%; however, specificity is limited by persistent detection of noninfectious viral RNA.4,5,7

The Centers for Disease Control and Prevention advises that immune-competent adults are not infectious more than 10 days after symptom onset.7 RT-PCR testing detects noninfectious viral RNA up to 12 weeks after infection.7 To distinguish infectious from noninfectious virus, cycle thresholds may be used. The cycle threshold is the number of cycles a sample must be amplified in the laboratory before virus can be detected. A low cycle threshold value correlates with higher viral load and contagiousness because fewer cycles are required to detect virus. Cycle threshold values are also affected by collection technique and vary by assay, reducing their reliability.8

Application to This Patient

This patient had persistently positive RT-PCR test results for SARS-CoV-2 less than 90 days from prior infection. Because she remained asymptomatic, retesting provided no useful information. The Centers for Disease Control and Prevention recommend that patients infected within the past 90 days without new COVID-19 symptoms should not be retested.9 Reinfection with SARS-CoV-2 is rare (risk of reinfection, 0.17%).10 However, whether reinfection rates will increase due to Delta or other variants is unknown. There is no evidence of altered test performance with variants.

Patients undergoing asymptomatic screening have a pretest probability of COVID-19 that mirrors local prevalence. Thus, at the time of testing in this patient, the pretest probability of COVID-19 was approximately 0.35% (7-day cumulative average [0.07%] multiplied 5-fold to account for undertesting). Estimating 90% sensitivity and 95% specificity, the test positive predictive value was 24% but declined to approximately 0% given the patient’s recent history of COVID-19.

The ability of preprocedural testing to prevent nosocomial COVID-19 transmission varies with disease prevalence, infection history, the patient’s immunization status, employee vaccination rate, and personal protective equipment availability. Testing programs must consider what procedures have a high risk of transmission.
than 98%.4-6 Reported sensitivity of approximately 90% and specificity greater than 98%.

What Are Alternative Diagnostic Testing Approaches? Alternative tests include point-of-care antigen tests, which are less sensitive than RT-PCR but better predict contagiousness, indicated by correlation with viral culture and higher viral loads.4,6 Using viral culture as criterion standard, small studies of antigen tests have reported sensitivity of approximately 90% and specificity greater than 98%.4-6

Patient Outcome Consultation from an infectious disease specialist determined that the patient did not pose a transmission risk to medical staff. However, after further review the patient did not require endoscopic evaluation of the submucosal nodule for another 6 months, and the procedure was postponed.

### Table 2. Factors That Affect the Clinical Sensitivity or Specificity of SARS-CoV-2 Tests

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect on sensitivity or specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days from symptom onset</td>
<td>Sensitivity greatest at day 1-5 after symptom onset (&gt;90%), lower sensitivity earlier before symptoms or &gt;5 days after symptoms</td>
</tr>
<tr>
<td>Sampling site</td>
<td>Lower sensitivity for sampling sites other than nasopharyngeal</td>
</tr>
<tr>
<td>Antigen test compared with reverse transcriptase-polymerase chain reaction testing</td>
<td>Sensitivity: overall, 62%-64%; lower if asymptomatic; to detect likely contagious patients, 87%-90% sensitivity (lower if asymptomatic) Specificity: &gt;95%</td>
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(eg, intubation and bronchoscopy aerosolize particles from the respiratory tract and are associated with higher transmission risk) and balance transmission risk: reduction with potential harms to patients that result from delayed procedures following a positive test result.

### Clinical Bottom Line

- SARS-CoV-2 reverse transcriptase–polymerase chain reaction (RT-PCR) testing is highly sensitive (99%) but less specific (approximately 95%) for contagious COVID-19 and may be positive for ≥90 days after infection
- Viral antigen tests have lower analytic sensitivity than RT-PCR but are more specific for contagious disease
- Preprocedural COVID-19 testing can delay access to care, and testing asymptomatic low-risk patients undergoing an aerosol-generating procedure is not recommended when procedure-based personal protective equipment is available

### References


