Accuracy of Rapid Antigen vs Reverse Transcriptase–Polymerase Chain Reaction Testing for SARS-CoV-2 Infection in College Athletes During Prevalence of the Omicron Variant

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Introduction

One critical aspect of COVID-19 management has been to isolate or quarantine individuals to prevent viral spread. Reverse transcriptase–polymerase chain reaction (RT-PCR) tests are the criterion standard for diagnosis of SARS-CoV-2 infection but are limited by long turnaround times and complex laboratory methods.

Rapid antigen tests (RATs) can be performed and interpreted in minutes without the use of special equipment. With the rise of each new variant, the accuracy of RATs must be reevaluated. This case series evaluated the performance of RATs in detecting SARS-CoV-2 in the context of a dominant Omicron variant.

Methods

All Stanford University student athletes who reported no history of SARS-CoV-2 infection in the previous 90 days and returned to campus from January 1 through January 11, 2022, self-administered

Table. RAT vs RT-PCR Testing

<table>
<thead>
<tr>
<th>RAT result</th>
<th>RT-PCR–positive findings</th>
<th>RT-PCR–negative findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confirmed</td>
<td>Presumed</td>
</tr>
<tr>
<td>Positive, No. of participants</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Negative, No. of participants</td>
<td>27</td>
<td>0</td>
</tr>
</tbody>
</table>

Sensitivity, % (95% CI) [No./total No.:] 63.0 (51.9–74.1) [46/73] NA

Specificity, % (95% CI) [No./total No.:] NA 99.8 (99.5–100) [649/650]

Figure. SARS-CoV-2 Reverse Transcriptase–Polymerase Chain Reaction Cycle Threshold Values by Rapid Antigen Test (RAT) Results and COVID-19 Symptoms

![Graph showing cycle threshold values for symptomatic and asymptomatic athletes](image)

Data are from 723 student athletes undergoing testing for SARS-CoV-2. Solid lines indicate median cycle threshold value; dotted lines, cycle threshold value quartiles.

Abbreviations: NA, not applicable; RAT, rapid antigen testing; RT-PCR, reverse transcriptase–polymerase chain reaction.
an RAT (BinaxNOW; Abbott Laboratories) within 24 hours of campus arrival. Symptomatic students with a positive RAT result were isolated without confirmatory RT-PCR testing; asymptomatic students with a positive RAT result underwent RT-PCR testing (eMethods in the Supplement).

Statistical analysis was performed using Prism, version 9.0 (GraphPad Software), for data visualization and Mann-Whitney U tests for median cycle threshold (Ct) value comparison, with 2-sided P < .05 indicating statistical significance. This study was approved with a waiver of informed consent by the Stanford University Institutional Review Board. The reporting guideline for case series was used for this study.

Results
Participants included 723 students aged 17 to 23 years (376 [52.0%] female; 709 [98%] received 2-dose Pfizer or Moderna or 1-dose Johnson & Johnson vaccines). Forty-six participants (6.4%) had positive RAT findings, of whom 35 (76.1%) had symptomatic infections. Among these 35 participants, 12 received a positive RT-PCR result within 24 hours, whereas the remaining 23 were presumed to have positive results (Table). Twenty-seven participants had a negative RAT result followed by a positive RT-PCR result within 24 hours, for a total of 73 diagnosed SARS-CoV-2 infections in the included cohort (infectivity rate, 73 of 723 [10.1%]). Overall, RAT had a sensitivity of 63.0% (95% CI, 51.9%-74.1% [46 of 73]) and specificity of 99.8% (95% CI, 99.5%-100% [1 of 650]). Among symptomatic participants, RAT had a sensitivity of 77.8% (95% CI, 65.6%-89.9% [35 of 45]); among asymptomatic patients, 39.2% (95% CI, 21.2%-57.4%) [11 of 28]).

Participants with RAT- and RT-PCR-positive findings (n = 23) had a lower median Ct value of 24.6 (IQR, 22.2-32.3) compared with those with RAT-negative and RT-PCR-positive findings (n = 27), with a median Ct value of 35.0 (IQR, 29.8-36.6; P < .001) (Figure). In the RT-PCR-positive cohort, symptomatic individuals (n = 22) had lower Ct values compared with their asymptomatic counterparts (24.7 [IQR, 22.4-31.9] vs 33.6 [IQR, 29.3-35.7]; P = .004).

In the RT-PCR analysis, the Omicron variant represented 44 of 46 positive cases (95.7%). Four specimens could not be genotyped owing to low viral loads.

Discussion
The overall infectivity rate in our cohort was 10.1%, with 95.7% of infections due to the Omicron variant. The overall sensitivity of RAT was 63.0%, similar to that of 2 recent studies that also focused on the Omicron variant. Performance of RAT was better in symptomatic individuals, likely owing to the significant difference in Ct values, because Ct values have been shown to correlate to the sensitivity of RAT in both laboratory and clinical studies. Rapid antigen tests were quite specific, with only 1 false-positive finding in the cohort, suggesting that a positive RAT finding in both asymptomatic and symptomatic populations does not require confirmatory RAT or RT-PCR testing. This is consistent with previous studies that have shown excellent specificity.

Study limitations include self-administration and self-reporting of RAT findings, which could confound our results; however, RATs are frequently administered in this fashion. In addition, not every symptomatic patient with a positive RAT finding underwent confirmatory RT-PCR testing, which could cause elevated specificity values.

Rapid antigen testing performed similarly in the detection of the Omicron variant compared with previous variants, with high specificity but poor sensitivity, particularly among asymptomatic individuals. Its use as a screening tool for asymptomatic infection in the setting of widespread prevalence of the Omicron variant may be limited.
ARTICLE INFORMATION
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Author Contributions: Dr Hwang had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition, analysis, or interpretation of data: Tsao, Kussman, Costales, Pinsky, Hwang.
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Conflict of Interest Disclosures: Dr Kussman reported receiving personal fees from Fresno Madera Medical Society outside the submitted work. Dr Abrams reported owning stock or stock options from AxGen and Cytonics; serving as a board or committee member for the American Academy of Orthopaedic Surgeons, American Orthopaedic Society for Sports Medicine, and International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine; receiving cadaver labs and equipment for educational purposes from Arthrex and Stryker; receiving consulting fees from Bioventus Inc, Cytonics, Fidia Pharma, and RubiconMD; and serving as an unpaid consultant for TeachAids. No other disclosures were reported.
REFERENCES
SUPPLEMENT.
eMethods. Reverse Transcriptase-Polymerase Chain Reaction Testing
eReferences