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Low Sensitivity of Rapid Antigen Tests to Detect Severe Acute Respiratory Syndrome Coronavirus 2 Infections Before and on the Day of Symptom Onset in Nursing Home Staff and Residents, Germany, January–March 2021

To the Editor—We read with interest the recent article by Smith et al [1], comparing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapid antigen detection tests (RADTs) with reverse-transcription quantitative polymerase chain reaction (RT-qPCR). Our observations obtained during a SARS-CoV-2 outbreak in a nursing home add further evidence regarding the reliability of RADTs.

RADTs provide a timely, easy-to-use, and crucial tool for detecting SARS-CoV-2 [2]. Thus, they are widely applied for routine screening at workplaces [3]. However, RADTs have a lower sensitivity than RT-qPCR [4]. Because RADTs were mostly validated in symptomatic cases, data on the sensitivity of RADTs when testing presymptomatic SARS-CoV-2 infections are limited [4, 5]. This is of great importance, however, because infectiousness is highest in the days before and around the time of symptom onset [6, 7]. Furthermore, presymptomatic transmission accounts for a substantial proportion of secondary cases [8].

In a cohort of RT-qPCR–confirmed SARS-CoV-2 alpha cases related to an outbreak in a nursing home in Germany in January–March 2021, we analyzed the sensitivity of a commercial RADT and of RT-qPCR, including 2 days before as well as the day of symptom onset ("reference period"). Nasopharyngeal samples were used for both RADTs and RT-qPCR and were collected by nursing home staff or external health professionals. RADTs were performed daily on staff, while residents were tested as needed (eg, after contact with a case). Furthermore, we assessed the association between a positive test result (RADT or RT-qPCR) and status (staff or resident), using the Fisher exact test.

Owing to multiple tests per person within the reference period, 35 RADT results were available from 18 individuals with coronavirus disease 2019 (8 residents and 10 staff; Table 1). Ten of the 35 RADTs had positive results (29% [95% confidence interval (CI), 15%–46%]). Remarkably, 6 of 8 RADTs (75%) performed on the day of symptom onset had negative results. Summarizing the results of all tests performed per case, RADTs identified 9 of 18 cases (50%) (8 of 8 residents [100%] and 1 of 10 staff [10%]). For RT-qPCR, 19 individual results were available (14 residents and 5 staff). Note that individuals who underwent RADTs did not necessarily undergo PCR within the reference period, and vice versa. RT-qPCR was performed only once for each case within the reference period and identified 17 of 19 cases (90% [95% CI, 67%–99%]; 13 of 14 residents [93%] and 4 of 5 staff [80%]). RT-qPCR results did not differ between residents and staff ($P = .46$), but staff were less likely than residents to have a positive RADT result (1 of 24 vs 9 of 11, respectively; $P < .01$).

Our study is limited by its small sample size. We had too few observations to investigate the effect of vaccination or the day of testing relative to symptom onset. Furthermore, we could not directly compare RT-qPCR and RADT results because the study populations differed.

In line with the higher sensitivity of RT-qPCR relative to RADTs in the early infectious period, as described by Smith et al [1], our analyses show that RT-qPCR identified cases before or on the day of symptom onset more reliably than RADTs. Only 29% of all RADTs performed within the reference period yielded a true-positive result, even though high viral loads are expected at this time [6, 9]. Our results are also in accordance with a recent Cochrane review, which demonstrated a low sensitivity of 58.1% (95% CI, 40.2%–74.1%) for RADTs in asymptomatic, PCR-confirmed SARS-CoV-2 cases [5]. However, that review did not assess sensitivity in presymptomatic cases.

We observed a higher proportion of positive RADTs among residents than among staff. In contrast, the sensitivity of RT-qPCR was similar in both groups. For RT-qPCR, health workers from outside the nursing home performed the sampling. For the RADTs, swab samples were obtained by nursing home staff, and it was reported that they were well trained and that sampling was performed similarly for staff and residents. Nonetheless, sampling differences, such as hesitancy to perform deep swabbing on colleagues, cannot be ruled out and could explain the lower sensitivity among staff. Likewise, sampling differences could partially

Table 1. Test Results in Samples Obtained at and Before Symptom Onset From Nursing Home Staff and Residents Positive for Severe Acute Respiratory Syndrome Coronavirus 2 in an Alpha Variant Outbreak, Germany, January–March 2021

	Samples by Test Result, No. (%)[a]							
	Day 0		Day −1		Day −2		Total	
Test	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
RADT[b]	2 (25)	6 (75)	1 (10)	9 (90)	7 (41)	10 (59)	10 (29)	25 (71)
Staff	1 (14)	6 (86)	0	8 (100)	0	9 (100)	1 (4)	23 (96)
Residents	1 (100)	0	1 (50)	1 (50)	7 (88)	1 (12)	9 (82)	2 (18)
RT-qPCR[c]	5 (100)	0	9 (90)	1 (10)	3 (75)	1 (25)	17 (90)	2 (10)
Staff	3 (100)	0	0	0	1 (50)	1 (50)	4 (80)	1 (20)
Residents	2 (100)	0	9 (90)	1 (10)	2 (100)	0	13 (93)	1 (7)

Abbreviations; RADT, rapid antigen detection test; RT-qPCR, reverse-transcription quantitative polymerase chain reaction.

[a]Percentages are row percentages for each day. Day 0 was the day of symptom onset; days −1 and −2, the presymptomatic period.

[b]RADTs were repeatedly performed within the reference period (35 results were available from 18 cases).

[c]RT-qPCR was performed only once for each case within the reference period (19 results available from 19 cases); note that RT-qPCR and RADT results are not necessarily derived from the same individuals and thus represent different study populations.

explain the higher sensitivities found by Smith et al [1], in a study where study staff collected the samples.

As highlighted in our study, RADT sensitivity is low before and on the day of symptom onset. Even with increased test frequency, sensitivity reached only 50%. This is particularly worrisome in the light of a decision adopted by the German federal government and Länder (federal states) on 23 August 2021 to permit social gatherings (eg, visits to mass events) with a single negative RADT result <24 hours old [10]. A negative RADT result must be interpreted cautiously, and nonpharmaceutical preventative measures must remain implemented, especially among vulnerable groups.

We obtained our results during an outbreak investigation conducted as part of the official tasks of the respective district's. Local public health authorities, supported by the Robert Koch Institute on official request in accordance with section 4 of the German Protection Against Infection Act. This investigation was therefore exempt from additional institutional review.

Notes

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Response to Bender et al

To the Editor—We thank the authors for their interesting letter. We would be most interested in knowing the exact brand of rapid antigen detection test (RADT) they utilized, as these tests can vary in both sensitivity and reliability. We would also be interested in seeing their individual-level timing of tests and results; given the wide variety of testing times and frequencies, it is difficult to determine which results are comparable with our daily sampling. However, in general, it would be difficult to compare these results because of the limited prescreening employed in the Bender et al study. One of the most important aspects of our study was a negative polymerase chain reaction (PCR) result in the previous 7 days, ensuring that all people enrolled in our study were newly infected [1]. As it is well known that quantitative reverse transcription PCR (RTqPCR) results can remain positive long after a mildly symptomatic or asymptomatic infection [2], and as we have shown that RADTs will rapidly turn negative after the infectious period has passed, it is possible that some participants in the study described by Bender et al were not newly infected and, therefore, would not be expected to have a positive RADT. Ensuring that participants are early in their infection is essential for accurate estimation of test sensitivity for SARS-CoV-2 infection, and we encourage anyone designing a test validation trial to consider this point carefully.

Notes

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