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Technical Note

Comparison of SARS-CoV-2 antigen testing to RT-PCR in a real-world setting—an observational cohort study

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ABSTRACT

A total of 2978 patients with validated paired results (SARS-CoV2-antigen and PCR) were identified. Our results show that only 45 antigen tests from 90 patients with positive validated PCR were correctly identified by antigen testing (sensitivity 50%). Roughly 50% of these patients had ongoing respiratory symptoms.

The ongoing CoV2 pandemic with its economic and educational considerations led to an understandable debate about the end of restrictions with the now ubiquitous availability of vaccinations. In addition to the RT-PCR as the state-of-the art detection method, antigen testing has become a very popular tool in the effort to relieve restrictions and reopen society. In anticipation of widespread antigen testing, it has been perceived by the public as a diagnostic tool with a high standard of safety and diagnostic accuracy. The proportion of false negatives is a well-established problem that must be kept in mind when considering the easing of restrictions on the population during this pandemic (Krüttgen et al., 2021; Lindner et al., 2021). There are many factors which determine the accuracy of antigen testing (Ciotti et al., 2021; Dinnes et al., 2021). To describe the situation of broad antigen testing as part of an "end-of-restriction" strategy, we analyzed a large cohort of subjects in a low incidence area retrospectively, to illustrate such a real-world testing scenario.

Between October 21, 2020 and March 8, 2021, all patients admitted to 3 tertiary hospitals were tested with antigen test and RT-PCR as part of the local testing strategy. Because of the observational character of the study no ethical committee review was necessary. Hospital admissions were based on several factors including ambulatory surgery, planed diagnostic interventions or for emergency reasons. Antigen tests and collections of RT-PCR test samples were gathered simultaneously within 24 hours and obtained by the same technique (nasopharyngeal swab) utilizing different antigen test kits (Roche, Nal-von Minden, Lyher) and RT-PCR tests (Cepheid GeneExpert, Roche, Fisher Scientific, Altona Diagnostics). Through this approach a total of 2978 patients with validated paired results were identified. One-third had respiratory symptoms with a frequently appearing underlying disease which potentially affected the lung (hearth failure, COPD, metabolic disorders). Table 1 shows the results of the antigen/RT-PCR pairs of our study group.

The positive predictive value was 0.68, and negative predictive value was 0.99. The sensitivity/ true positive rate was 0.5. Our results show that only 45 antigen tests from 90 patients with positive validated PCR were correctly identified by antigen testing. Roughly 50% of these patients had ongoing respiratory symptoms. Asymptomatic carriers of SARS-CoV-19 as well as subjects with transmission potential could have led to a higher false-negative rate.

To our knowledge, this is the biggest observational study to date investigating the safety of antigen testing compared to PCR in a real-world environment. We found true positive antigen-based results only in the half of our general mostly asymptomatic population with a RT-PCR-based confirmation of a SARS-CoV-2 infection. Patients with positive PCR results were roughly in 50% symptomatic.

In the literature antigen test sensitivities in symptomatic patients lie in between 72.0% and 78, 3% (Dinnes et al., 2021; Ferguson et al., 2020; Krüttgen et al., 2021). Antigen test sensitivity is highest in symptomatic people in the first week of infection. In symptomatic patients the antigen tests are useful if immediate results are required or RT-PCR is not available. False-negative results should be questioned in patients with clinical signs of COVID-19. The evidence of antigen testing in asymptomatic cohorts is limited with an average sensitivity of 58% (Dinnes et al., 2021).

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Table 1
Paired results of antigen test and RT-PCR in the whole cohort.

	Ag neg PCR neg	Ag neg PCR pos	Ag pos PCR neg	Ag pos PCR pos
N absolute	2867	45	21	45
Relative	96.3%	1.5%	0.7%	1.5%

In mixed populations with a high percentage of asymptomatic people the sensitivity of antigen tests is poorly described. The (mass) antigen test allows to screen at-risk populations and could allow faster return to working places or other institutions. The situation of a low incidence and a high percentage of asymptomatic people illustrates best the current worldwide situation and our study setting. In addition, our testing strategy described above may be of value as a mass screening in a population at higher risk for infection. Our study reflects the current situation in 3 hospitals and provides evidence of future testing strategies for these institutions. The results are in line with studies in asymptomatic cohorts (Dinnes et al., 2021). Our results provide evidence of usefulness and limitations of antigen tests and leads to several implications.

Symptomatic people with negative antigen tests should be handled with caution and should in addition undergo RT-PCR testing. In the ongoing pandemic antigen testing should be combined with established protection policies to maximize “anti-pandemic” effects. The low sensitivity of antigen tests in asymptomatic persons as demonstrated by our study and the growing general availability of antigen testing may give rise to an unwarranted carelessness. The results of our study may help to calculate the risk of an antigen-based testing strategy more accurately and provide a base for an “opening strategy” in the ongoing pandemic.

Author contributions

All authors contributed to the design and implementation of the research, to the analysis of the results and to writing of the manuscript.

JB is the guarantor of the paper, taking responsibility for the integrity of the work as a whole, from inception to published article.

Declaration of competing interest

All authors declare no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.diagmicrobio.2021.115531.

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