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Diagnostic accuracy of a novel SARS CoV-2 rapid antigen test and usefulness of specimens collected from the anterior nasal cavity

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ABSTRACT

Objectives: We aimed to validate a newly developed antigen-detecting rapid diagnostic test (Ag-RDT) for SARS-CoV-2 using anterior nasal specimens.
Methods: Between February 12 and September 30, 2021, 16 patients (age range, <1 month-76 years) were enrolled, and samples were collected simultaneously from anterior nasal and nasopharyngeal sites continuously during hospitalization. The primary end points were the diagnostic accuracy of the Ag-RDT and utility of anterior nasal specimens.
Results: In total, 226 sets of paired samples were obtained. In 88.2% of specimens, the viral load was high at the nasopharyngeal site. The mean cycle threshold values for the anterior nasal and nasopharyngeal sites were 32.4 and 29.9, respectively. Using the real-time polymerase chain reaction results as a reference, the Ag-RDT showed a 100% sensitivity up to day 6 of the illness, using specimens with moderate or high viral load (cycle threshold <30) from either site. From day 7, the sensitivity was 70.4-90.6% and 83.9-84.6% for the anterior nasal and nasopharyngeal sites, respectively. The specificity remained at 100%.
Conclusion: Our novel Ag-RDT meets the World Health Organization criteria and provides stable sensitivity and specificity and accurate results with anterior nasal specimens.

1. Introduction

Many health care providers are hopeful regarding COVID-19 testing programs that use accurate rapid antigen tests to reduce the burden on the health care system through early diagnosis of infection (Chen *et al.*, 2021). If performed appropriately, these testing programs can support rapid and accurate decisions with respect to the isolation and treatment of patients with COVID-19 (World Health Organization, 2020a). Currently, various antigen-detecting rapid diagnostic tests (Ag-RDTs) for SARS-CoV-2 are commercially available (Brümmer *et al.*, 2021; Foundation of Innovative new diagnosis (FIND), 2022; Kobayashi *et al.*, 2021; Krüttgen *et al.*, 2021; Lambert-Niclot *et al.*, 2020; Mak *et al.*, 2021; Osterman *et al.*, 2021; Porte *et al.*, 2020). Compared with laboratory-based reverse transcription-polymerase chain reaction (RT-PCR), which is the gold standard (Sethuraman *et al.*, 2020), Ag-RDTs require less technical expertise and laboratory capacity. Moreover, Ag-RDT results are delivered within 10-30 minutes and are available within a single clinical encounter (Brümmer *et al.*, 2021; Dinnes *et al.*, 2021). Thus, Ag-RDTs may overcome the drawbacks of RT-PCR in terms of availability, throughput, and turnaround time. The limitations of RT-PCR are recognized as major barriers to the broad implementation of urgent testing. Early diagnosis of COVID-19 and timely isolation are most often addressed by testing individuals

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with symptoms or known exposure to individuals who tested positive. Testing facilities aimed at confirming or ruling out COVID-19 in this population are affiliated with various primary and secondary care facilities. More recently, as point-of-care devices, tests can be performed by minimally trained individuals or self-taught individuals in a community setting, and self-testing is also being applied (Mahase, 2020; Mistry *et al.*, 2021).

The widespread use of testing outside medical institutions suggests that anterior nasal specimens, which can be safely self-collected by the patient, are now being used instead of nasopharyngeal specimens collected by medical staff (Lambert-Niclot *et al.*, 2020). Therefore, to evaluate the usefulness of specimens collected from the anterior nasal cavity, understanding the viral load and diagnostic accuracy of tests performed using anterior nasal specimens is vital. Furthermore, to assess the accuracy of Ag-RDTs in diagnosing COVID-19, diagnostic accuracy studies must be conducted in defined clinical settings. However, insufficient studies have been conducted to date. Initial data from independent evaluations suggest that the performance of SARS-CoV-2 Ag-RDTs may be inferior to that reported by the manufacturers, particularly in samples collected several days after disease onset (Brümmer *et al.*, 2021).

In this study, we aimed to evaluate the diagnostic accuracy of the newly developed Ag-RDT, RapidTesta SARS-CoV-2 (Sekisui Medical Co., Ltd., Japan) (Sekisui Medical Co., Ltd., 2022) for diagnosing COVID-19, using anterior nasal specimens in a designated medical institution for treating COVID-19.

2. Methods

2.1. Participants

This prospective cross-sectional study was conducted at the Emergency Center and Intensive Care Unit at Jichi Medical University Hospital and Jichi Children's Medical Center in Tochigi, Japan from February 12, 2021 to September 30, 2021. The participants of this study were patients who were hospitalized with a fever above 37.5°C and a positive SARS-CoV-2 RT-PCR test result using nasopharyngeal specimens analyzed in our hospital laboratory. Mild disease was defined as oxygen saturation maintained above 93%, without supplemental oxygen, and moderate-to-severe disease was defined as oxygen saturation below 93%, with pneumonia findings, requiring supplemental oxygen or mechanical ventilation. The exclusion criteria were as follows: (i) inability or unwillingness to provide informed consent, (ii) bleeding disorder, (iii) pregnancy or lactation, (iv) no preexisting indication for SARS-CoV-2 testing, and (v) symptom onset >10 days before the initial testing day. All experiments on human participants were performed in accordance with the Declaration of Helsinki, and all participants or their parents or guardians provided written informed consent. The protocol was approved by the institutional review board of Jichi Medical University Hospital on February 3, 2021 (approval no. 21-030).

2.2. Testing procedures

We conducted our study to determine the diagnostic performance of the RapidTesta SARS-CoV-2 test and compare it with that of RT-PCR, using specimens collected from the anterior nasal and nasopharyngeal sites. Furthermore, ESPLINE SARS-CoV-2 (Fujirebio Co., Ltd., Japan), an Ag-RDT that has been marketed and widely used since May 2020, was used as a comparator representing the efficacy of common Ag-RDTs. The sensitivity and specificity of ESPLINE SARS-CoV-2 are stated in the package insert as 93.8% and 100%, respectively, for nasopharyngeal specimens and 83.9% and 100%, respectively, for nasal specimens (Fujirebio Co., Ltd., 2021). Four specimen swabs were taken simultaneously from each patient on admission: an anterior nasal and nasopharyngeal specimen from each nostril and repeat samples when consent was obtained from the patient or parent or guardian of the patient. The anterior nasal and nasopharyngeal specimens were collected as previously described (Marty et al., 2020; Spyridaki et al., 2009). To eliminate variations due to specimen collection techniques, all specimens were collected by the same physician. Ag-RDT analysis was performed within 1 hour of specimen collection in a biosafety level 2 laboratory safety cabinet. The specimens were immersed in the buffer solution provided with the Ag-RDTs, the buffer solution was dropped into the small window of the device, and the test results were read after completion of the incubation period by visual assessment. To judge the RapidTesta SARS-CoV-2 results objectively, we evaluated the results using the RapidTesta Reader after visual assessment, as shown in Figure S1. The residual buffer was stored at -80°C within 1 hour after Ag-RDT and used for real-time RT-PCR testing. RNA extraction was performed using the QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany) with a 140-µl aliquot of each sample. A one-step RT-PCR (Thermo Fisher Scientific, MA, USA), which targets nucleotide 2 gene-specific primers for SARS-CoV-2, was performed according to the manufacturer's instructions (Spyridaki et al., 2009) and the National Institute of Infectious Disease protocols (National Institute of Infectious Disease, 2020). The cycle threshold (Ct) cutoff value for RT-PCR to determine antigen positivity in the Ag-RDTs was ≤30.0. If the Ct value was >30.0, the RT-PCR was repeated twice, and the Ct value was calculated again for confirmation (National Institute of Infectious Disease, 2020). Even in RT-PCR, the accuracy of the test is reduced according to the amount of virus in the specimen, resulting in false-negative results. Therefore, evaluating the Ct value with respect to the viral load is crucial (Rabaan et al., 2021). The Ct value of the detection limit of the Ag-RDT was determined from the mean value of false-negative samples. Mutation analysis using TaqMan SARS-CoV-2 mutation panels (Applied Biosystems, Foster City, MA, USA) was performed according to the manufacturer's instructions (Thermo Fisher Scientific, 2022), as shown in Table S1. The results of Ct values and mutations were analyzed using the CFX Maestro software package (Bio-Rad, Hercules, MA, USA).

2.3. Statistical analyses

All statistical analyses were performed using the R software program version 4.1.0 (www.r-project.org) (R Foundation for Statistical Computing, Vienna, Austria). The sensitivity and specificity values of the Ag-RDT results were calculated using the Clopper and Pearson method with 95% confidence intervals. Sensitivity comparisons between SARS-CoV-2 variants were performed using Fisher's exact test. The Ct values of the anterior nasal and nasopharyngeal specimens were calculated using the Wilcoxon rank-sum test.

3. Results

A total of 16 (four pediatric and 12 adult) patients were included in this study, and their ages ranged from less than 1 month to 76 years (Table 1). The mean and median ages were 35 and 37 years, respectively. A total of 226 pairs of anterior nasal and nasopharyngeal specimens were collected from the patients who were hospitalized. All enrolled patients were febrile (temperature >37.5°C) within 3 days of disease onset. On admission, 81% of the patients had upper respiratory symptoms, such as cough and nasal discharge, 13% had lower respiratory symptoms, such as wheezing, and 31% had respiratory distress. All adult patients had moderate-to-severe disease at admission, and all patients were treated with remdesivir (200 mg intravenous injection on the first day and 100 mg on the second and subsequent days) and dexamethasone (6 mg intravenously once daily for 4-6 days), except patient 8, in accordance with patient and family wishes. Tocilizumab (400-800 mg,

Table 1
Summary of the characteristics, clinical course, and treatment of the participants.

Patient no.	Age (years/ months)	Days from onset to hospitalization	SARS-CoV-2 variant	Clinical manifestations				Therapy		
				Cough	Nasal discharge	Respiratory distress	Wheezing or crackles	Remdesivir	Dexamethasone	Tocilizumab
1	76 y	9	NA	+[a]	+	+	+	+	+	
2	28 y	7	B.1.1.33					+	+	
3	4 y	5	B.1.1.33		+					
4	4 m	6	B.1.1.33		+					
5	25 y	9	Alpha					+	+	
6	46 y	2	Alpha	+	+			+	+	
7	57 y	6	B.1.1.33					+	+	
8	23 y	2	B.1.1.33	+	+					
9	2 y	6	Alpha	+	+					
10	69 y	7	Alpha	+	+	+	+	+	+	+
11	50 y	5	B.1.1.207 or B.1.177	+	+	+		+	+	+
12	1 m	3	Delta	+	+					
13	25 y	1	Delta	+	+			+	+	+
14	56 y	9	Delta	+	+	+		+	+	+
15	48 y	9	Delta	+				+	+	+
16	52 y	8	Delta	+		+		+	+	+

[a] Reported or observed. Abbreviations: m, months; y, years.

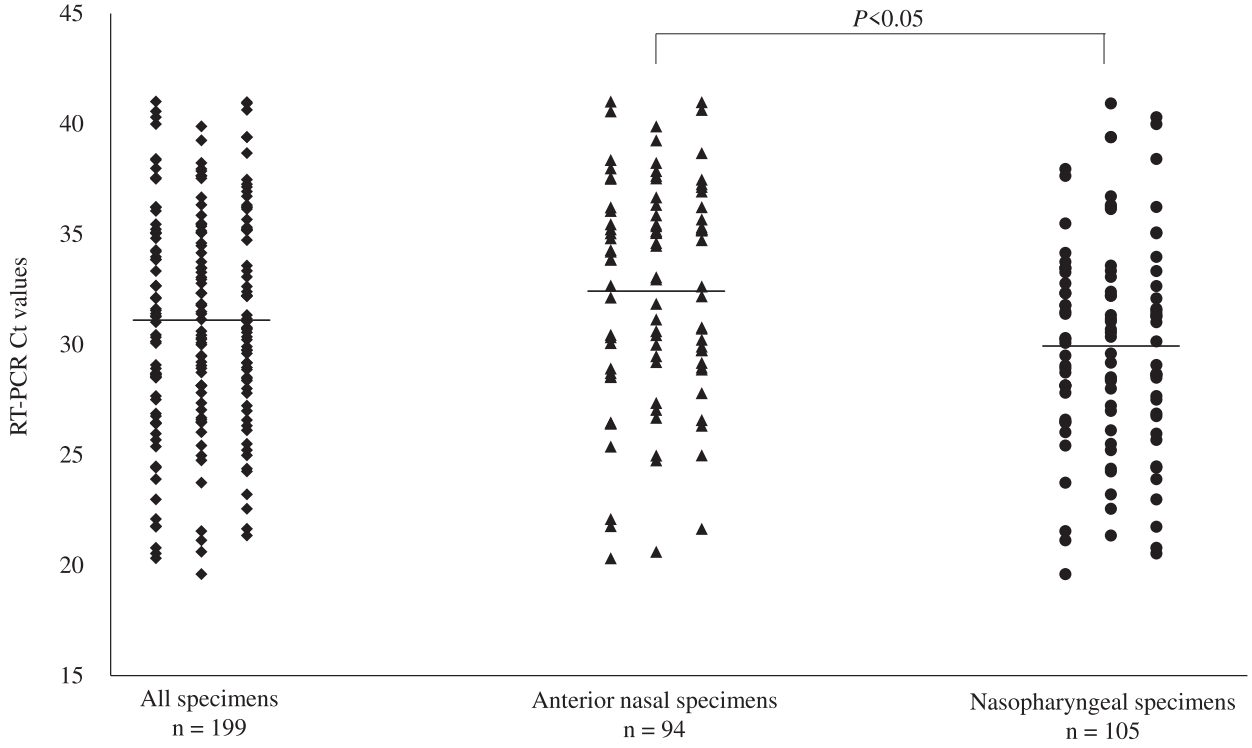

Figure 1. Comparison of RT-PCR Ct values for the collected samples. The Ct values of specimens that were positive for SARS-CoV-2 antigen by RT-PCR are analyzed. The mean Ct value for all specimens is 31.1 (range: 19.6-41.0), the mean Ct value for anterior nasal specimens is 32.4 (range: 20.3-41.0), and the mean Ct value for nasopharyngeal specimens is 29.9 (range: 19.6-40.9). Mean Ct values are shown as horizontal bars.
Abbreviations: Ct, cycle threshold; RT-PCR, reverse transcription-polymerase chain reaction.

body weight equivalent) was also used as therapy in six patients with moderate-to-severe disease within 9 days of onset. These drugs were not used in pediatric patients due to the lack of established safety and efficacy data. The respiratory status of all patients was assessed. Oxygen was administered for dyspnea or if oxygen saturation fell below 93%, and ventilator or extracorporeal membrane oxygenation management was provided if necessary, depending on the status of respiratory failure. All 12 adult patients were placed on ventilator management due to worsening respiratory status. In addition, extracorporeal membrane oxygenation was administered to adult patients 1 and 10 (approximately 16%). The new-born patient aged 1 month was the only pediatric patient treated with oxygen. Among all specimens, the mean Ct value in patients with positive RT-PCR results was 31.1 (range: 19.6-41.0), the mean Ct value of the anterior nasal specimens was 32.4 (range: 20.3-41.0), and the mean Ct of the nasopharyngeal specimens was 29.9 (range: 19.6-40.9) (Figure 1). Moreover, among the positive RT-PCR specimens, 88.2% of anterior nasal specimens had higher Ct values than those of the nasopharyngeal specimens. The Ct value of the anterior nasal specimens remained at approximately 32 from the time of onset to day 16 of illness, whereas that of the nasopharyngeal specimens tended to gradually

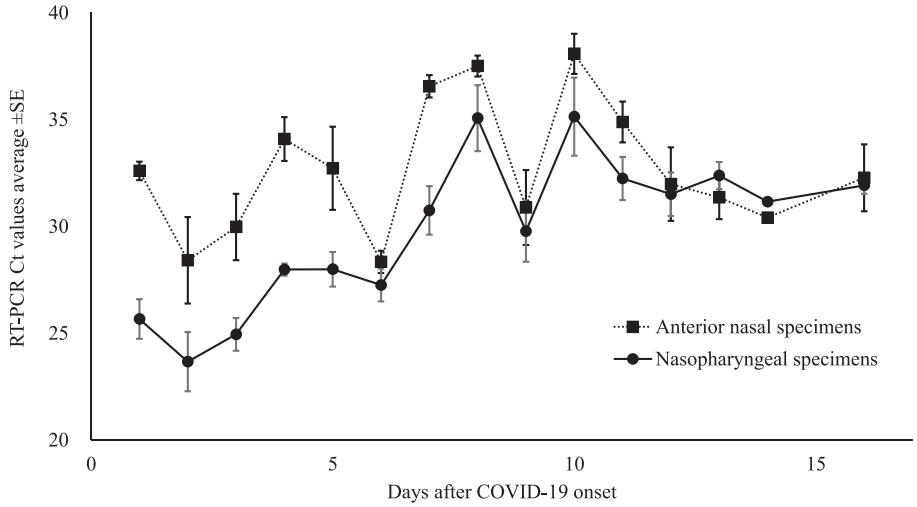

Figure 2. Comparison of RT-PCR Ct values of specimens collected over time from COVID-19 onset. The Ct values of the anterior nasal and nasopharyngeal specimens collected over time after COVID-19 onset are shown. In the anterior nasal specimens, there is no significant difference in the Ct values on day 1 after onset and day 16 after onset. There is also no significant difference in the Ct value of the nasopharyngeal specimens by time since onset.
Abbreviations: Ct, cycle threshold; RT-PCR, reverse transcription-polymerase chain reaction.

Table 2
Diagnostic accuracy of two antigen-detecting rapid diagnostic tests for SARS-CoV-2 using anterior nasal and nasopharyngeal specimens.

		Sensitivity (%)	95% CI	Specificity (%)	95% CI	Detection limit by cycle threshold value
RapidTesta	Anterior nasal specimens	81.9% (77/94)	72.6-89.1%	100% (19/19)	82.4-100%	41.0
SARS-CoV-2	Nasopharyngeal specimens	89.5% (94/105)	82.0-94.7%	100% (8/8)	63.1-100%	40.3
RapidTesta Reader	Anterior nasal specimens	88.3% (83/94)	80.0-94.0%	100% (19/19)	82.4-100%	41.0
	Nasopharyngeal specimens	89.5% (94/105)	82.0-94.7%	100% (8/8)	63.1-100%	40.3
ESPLINE	Anterior nasal specimens	77.7% (73/94)	67.9-85.6%	100% (19/19)	82.4-100%	41.0
SARS-CoV-2	Nasopharyngeal specimens	81.9% (86/105)	73.2-88.7%	100% (8/8)	63.1-100%	40.3

All specimens are visually evaluated with RapidTesta SARS-CoV-2 and immediately read using a RapidTesta Reader. Visual analysis of ESPLINE SARS-CoV-2 is performed simultaneously with RapidTesta SARS-CoV-2.

Table 3
Summary of the sensitivity of antigen-detecting rapid diagnostic test according to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant.

		Alpha		Delta		Other	
		Sensitivity (%)	95% CI	Sensitivity (%)	95% CI	Sensitivity (%)	95% CI
RapidTesta	Anterior nasal specimens	77.4% (24/31)	(58.9-90.4%)	92.3% (24/26)	(74.9-99.1%)	78.4% (29/37)	(61.8-90.2%)
SARS-CoV-2	Nasopharyngeal specimens	82.5% (33/40)	(67.2-92.7%)	92.3% (24/26)	(74.9-99.1%)	94.9% (37/39)	(82.7-99.4%)
RapidTesta	Anterior nasal specimens	80.6% (25/31)	(62.5-92.5%)	92.3% (24/26)	(74.9-99.1%)	91.9% (34/37)	(78.1-98.3%)
Reader	Nasopharyngeal specimens	82.5% (33/40)	(67.2-92.7%)	92.3% (24/26)	(74.9-99.1%)	94.9% (37/39)	(82.7-99.4%)
ESPLINE	Anterior nasal specimens	71.0% (22/3)	(52.0-85.8%)	76.9% (20/26)	(56.4-91.0%)	83.8% (31/37)	(68.0-93.8%)
SARS-CoV-2	Nasopharyngeal specimens	77.5% (31/40)	(61.5-89.2%)	88.5% (23/26)	(69.8-97.6%)	82.1% (32/39)	(66.5-92.5%)

increase from 25 to 32 over time. A comparison of Ct values of the anterior nasal specimens on days 1 and 16 of illness did not show a significant difference, and the same was true for nasopharyngeal specimens (Figure 2).

In the anterior nasal specimens, the sensitivity and specificity of RapidTesta SARS-CoV-2 were 81.9% and 100%, respectively (Table 2). In the nasopharyngeal specimens, the sensitivity and specificity were 89.5% and 100%, respectively. The detection limit of the Ct value was 41.0. The mean Ct values of the anterior nasal and nasopharyngeal specimens of each subtype were 30.2 ± 0.8 and 28.3 ± 0.7, respectively, for the Delta strain; 32.5 ± 0.9 and 28.9 ± 0.8, respectively, for the Alpha strain; and 35.4 ± 0.5 and 31.4 ± 1.0, respectively, for the other strains. A low viral load in a specimen may result in a negative result, that is, a false-negative, by visual judgment. On the other hand, RapidTesta Reader is highly likely to provide a positive result, even for specimens with low viral load that are judged as false-negatives by visual judgment. Comparison of sensitivity by visual judgment between SARS-CoV-2 subtypes using Fisher's exact test showed no difference (Table 3). However, regarding the sensitivity of anterior nasal specimens of Alpha and other strains, which have a low viral load derived from the Ct values, there was a divergence in the results: negative by visual judgment and positive by RapidTesta Reader (Table 3). The sensitivities of the comparator, ESPLINE SARS-CoV-2, were 77.7% in anterior nasal specimens and 81.9% in the nasopharyngeal specimens, and the detection limit Ct value was 41.0.

The rate of Ag-RDT positivity decreased with the course of the disease, as shown in Table 4. Sensitivity stabilized until 6 days after onset, remaining at 100% using both the anterior nasal spec-

Table 4
Summary of antigen-detecting rapid diagnostic test for SARS-CoV-2 sensitivity and specificity by days since COVID-19 onset.

		<6 days			7–9 days			>10 days		
		Sensitivity	95%CI	Specificity 95%CI	Sensitivity	95%CI	Specificity	95%CI	Sensitivity	95%CI	Specificity	95%CI
RapidTesta SARS-CoV-2	Anterior nasal specimens	100% (35/35)	(90.0–100%)	NA	55.6% (15/27)	(35.3–74.5%)	100% (3/3)	(29.2–100%)	84.4% (27/32)	(67.2–94.7%)	100% (5/5)	(47.8–100%)
	Nasopharyngeal specimens	100% (35/35)	(90.0–100%)	NA	83.9% (26/31)	(66.3–94.5%)	100% (7/7)	(59.0–100%)	84.6% (33/39)	(69.5–94.1%)	100% (12/12)	(73.6–100%)
RapidTesta Reader	Anterior nasal specimens	100% (35/35)	(90.0–100%)	NA	70.4% (19/27)	(49.8–86.2%)	100% (3/3)	(29.2–100%)	90.6% (29/32)	(75.0–98.0%)	100% (5/5)	(47.8–100%)
	Nasopharyngeal specimens	100% (35/35)	(90.0–100%)	NA	83.9% (26/31)	(66.3–94.5%)	100% (7/7)	(59.0–100%)	84.6% (33/39)	(69.5–94.1%)	100% (12/12)	(73.6–100%)
ESPLINE SARS-CoV-2	Anterior nasal specimens	97.1% (34/35)	(85.1–99.9%)	NA	51.9% (14/27)	(31.9–71.3%)	100% (3/3)	(29.2–100%)	78.1% (25/32)	(60.0–90.7%)	100% (5/5)	(47.8–100%)
	Nasopharyngeal specimens	100% (35/35)	(90.0–100%)	NA	74.2% (23/31)	(55.4–88.1%)	100% (7/7)	(59.0–100%)	71.8% (28/39)	(55.1–85.0%)	100% (12/12)	(73.6–100%)

NA: Not applicable.

imens and nasopharyngeal specimens, and the sensitivity of both sites decreased with time after onset. The sensitivity of the anterior nasal specimens began to be inferior to that of the nasopharyngeal specimens 7 days after onset, but even 10 days after onset, the sensitivity remained above 90%. The RapidTesta Reader contributed to the improvement in sensitivity, and the sensitivities in the anterior nasal specimens were increased by 14.8% 7-9 days after onset and 6.2% 10 days after onset (Table 4). False-negative results for RapidTesta SARS-CoV-2 were observed in both the anterior nasal and nasopharyngeal specimens ≥7 days after onset. In the anterior nasal specimens, the false-negative rates were 29.6% on days 7-9 of illness and 9.4% after day 10 of illness. In the nasopharyngeal specimens, these values were 16.1% and 15.4%, respectively (Table 4). Therefore, the use of the RapidTesta Reader contributed to the high accuracy of the RapidTesta SARS-CoV-2 test in the assessment of specimens with higher Ct values ≥7 days after onset.

4. Discussion

The results revealed that the newly developed Ag-RDT for COVID-19 had high diagnostic accuracy, and that specimens collected from the anterior nasal cavity could be used as an alternative to nasopharyngeal specimens. Because the amount of virus is proportional to the coloration intensity of the Ag-RDT judgment line, it should be noted that a lower amount of virus in the specimen is correlated with a lower positivity rate by visual judgment; thus, the visual judgment and RapidTesta Reader results may diverge. A recent systematic review and meta-analysis reported that the mean sensitivity of Ag-RDTs at 1 week after COVID-19 onset was high (78-84%) (Brümmer *et al.*, 2021; Dinnes *et al.*, 2021). We demonstrated that the diagnostic accuracy of a newly developed Ag-RDT, RapidTesta SARS-CoV-2, with the use of anterior nasal specimens, had a sensitivity of 100% in the first week after onset and 88.3% in all specimens until day 16 after onset, meeting the World Health Organization criterion of ≥80% sensitivity (World Health Organization, 2020a). The specificity of 100% for all specimens also met the World Health Organization criterion of ≥97% specificity (World Health Organization, 2020a). The sensitivity and specificity were both noninferior to those of the ESPLINE SARS-CoV-2. In specimens with a Ct value of ≤25, the sensitivity of Ag-RDTs increased to 94.5% (Dinnes *et al.*, 2021). In contrast, with RapidTesta SARS-CoV-2, the sensitivity remained at 100% at a Ct value of 28.5. Ag-RDTs are less sensitive than RT-PCR, and there are concerns about false-negative results. In terms of the association between false-negative results and Ct values, a Ct value of 30 is considered the threshold for the possibility of false-negative results on Ag-RDTs. This is because the average Ct value that is determined to be a false-negative result by Ag-RDTs is 31.9, and half of the clinical specimens are determined to give false-negative results by Ag-RDTs when the Ct value is above 30.0 (Lim *et al.*, 2022; Okoye *et al.*, 2022). False-negative results were found in 11.7% of all anterior nasal specimens with RapidTesta SARS-CoV-2, and the mean Ct value was 36.8. Even with specimens with high Ct values, which indicates a low viral load, RapidTesta SARS-CoV-2 had a relatively low rate of false-negative results.

Factors affecting the accurate diagnosis with Ag-RDTs should be emphasized, including the choice of specimen collection site and time after COVID-19 onset. In our data, the mean Ct value was approximately 1.1 times higher at the anterior nasal cavity than at the nasopharyngeal site. Although not a significant difference, this suggests that more viral replication of SARS-CoV-2 occurs in the nasopharynx, as reported previously (Centers for Disease Control and Prevention, 2021; World Health Organization, 2020b). The major factor that determines the sensitivity of Ag-RDTs is the viral load reflected in the Ct value, and the sensitivity decreases rapidly

to 51.0-61.5% in the second week after the onset as the viral replication decreases (Brümmer *et al.*, 2021; Dinnes *et al.*, 2021). Therefore, to maintain the sensitivity of Ag-RDTs, attention has been focused on the high viral load at the specimen collection site. This study found that the sensitivity of anterior nasal specimens in the second week of illness was 70.4-90.6%, which is satisfactory compared with that obtained with commercially available Ag-RDTs (Brümmer *et al.*, 2021; Dinnes *et al.*, 2021). Specimen collection from the anterior nasal cavity is not affected by the specimen collector's skill (Wölfl-Duchek *et al.*, 2022) or infection control and can even be performed by the patient, suggesting that this method is potentially useful for reducing the burden on medical staff.

This study had some limitations. First, Ct values and viral load may depend on the quality of the sample; that is, the method of collection and the swab used. In our study, all sampling was performed by the same physician, and the swabs used were those supplied with Ag-RDTs. Although this can be considered as a methodological strength with regard to variability of sampling, it is unclear whether there is variability in the results according to who collects the samples. Second, visual judgment bias may have been present. However, one of the two physicians who was not informed of the background of the specimens was allowed to make a decision. Third, the sensitivity of the Ag-RDTs was calculated for each day of illness; however, the number of samples in each group was small, so the statistical analyses may have been underpowered.

5. Conclusion

This study demonstrated the diagnostic accuracy of the newly developed RapidTesta SARS-CoV-2 test for the accurate diagnosis of COVID-19 in terms of both sensitivity and specificity. The anterior nasal cavity was shown to be useful as a specimen collection site. A review in the Cochrane Database of Systematic Reviews noted the importance of combined use of Ag-RDT and RT-PCR tests in the diagnosis of COVID-19 because the diagnostic accuracy of Ag-RDTs is limited (Dinnes *et al.*, 2021). This study demonstrates that RapidTesta SARS-CoV-2 has comparable sensitivity to RT-PCR for detecting SARS-CoV-2 in the early stages of COVID-19 and that anterior nasal specimens are useful. These results will provide an environment in which individuals are less hesitant and more willing to undergo Ag-RDT than in-person RT-PCR. The widespread use of Ag-RDTs with anterior nasal specimens has the potential to reduce the burden on medical staff.

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Ethical approval

All experiments on human participants were performed in accordance with the Declaration of Helsinki, and all participants or their parents provided written informed consent. The protocol was approved by the institutional review board of Jichi Medical University Hospital on February 3, 2021 (approval no. 21-030).

Declaration of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Daisuke Tamura: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Project administration, Funding acquisition. **Hirokazu Yamagishi:** Conceptualization, Methodology, Software, Validation, Writing – review & editing. **Yuji Morisawa:** Conceptualization, Writing – review & editing, Visualization. **Takashi Mato:** Conceptualization, Writing – review & editing. **Shin Nunomiya:** Conceptualization, Writing – review & editing. **Yuta Maehara:** Conceptualization, Writing – review & editing, Visualization. **Yasushi Ochiai:** Conceptualization, Writing – review & editing, Visualization. **Shinya Okuyama:** Conceptualization, Writing – review & editing, Visualization. **Narumi Ohmika:** Conceptualization, Writing – review & editing. **Takanori Yamagata:** Conceptualization, Writing – review & editing. **Hitoshi Osaka:** Conceptualization, Writing – review & editing, Supervision.

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Supplementary materials

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