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Comparison of the diagnostic sensitivity of SARS-CoV-2 nucleoprotein and glycoprotein-based antibody tests

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ABSTRACT

The emergence of the severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) has been followed by the rapid development of antibody tests. To assess the utility of the tests for clinical use and seroepidemiologic studies, we examined the sensitivity of commercial antibody tests from Roche, Abbott, Novatec, Virotech Siemens, Euroimmun, and Mediagnost in a prospective diagnostic study. The tests were evaluated with 73 sera from SARS CoV-2 RNA positive individuals with mild to moderate disease or asymptomatic infection. Sera were obtained at 2 – 3 weeks (N = 25) or > 4 weeks (N = 48) after symptom onset and viral RNA test. The overall sensitivity of the tests ranged from 64.4–93.2%. The most sensitive assays recognized 95.8–100 % of the sera obtained after 4 weeks or later. Sera drawn at 2 – 3 weeks were recognized with lower sensitivity indicating that the optimal time point for serologic testing is later than 3 weeks after onset of the disease. Nucleoprotein- and glycoproteinbased assays had similar sensitivity indicating that tests with both antigens are suitable for serological diagnostics. Breakdown of the test results showed that nucleoprotein- and glycoprotein-based tests of comparable sensitivity reacted with different sets of sera. The observation indicates that a combination of nucleoprotein- and glycoprotein-based tests would increase the percentage of positive results.

1. Introduction

Since its emergence in December 2019, the severe acute respiratory syndrome coronavirus (SARS-CoV)-2 has caused several million infections worldwide. IgG antibodies against the virus are a marker of previous infection. Information about the virus-specific IgG response is of relevance for public health because it informs about the level of exposure in the population. In addition, people having previously been diagnosed as SARS CoV-2-infected or being suspect of previous infection may want to know if they have antibodies against the virus. This information can be obtained by testing SARS-CoV-2-specific antibodies in serum samples. The accuracy of the results depends on the sensitivity and the specificity of the tests.

Several companies have developed SARS-CoV-2 antibody tests for laboratory use based on measuring antibodies against either the viral nucleoprotein or the glycoprotein [1–4]. The tests use different techniques such as sandwich enzyme immunoassays (EIA), chemiluminescence microparticle immunoassay (CMIA) and bridge immunoassays such as microparticle immunoassay (MIA) and electrochemiluminescence immunoassay (ECLIA). EIAs and CMIA use conjugated secondary antibody for detection of serum antibody. The MIA and ECLIA use a luminophor-conjugated viral antigen for antibody detection. The EIAs and the CMIA in this study measure single immunoglobulin classes, such as virus-specific IgG. The MIA and the ECLIA measure IgG and IgM and theoretically other antigen-specific immunoglobulins, as well.

The goal of the study was to examine and compare the sensitivity of seven commercial SARS CoV-2 antibody laboratory tests and to compare the reactivity pattern of virus nucleoprotein- and glycoprotein-based assays.

2. Study design

A prospective diagnostic study was initiated to evaluate the

Abbreviations: SARS, severe acute respiratory syndrome; EIA/ELISA, enzyme immunoassays; CMIA, chemiluminescence microparticle immunoassay; MIA, microparticle immunoassay; ECLIA, electrochemiluminescence immunoassay

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sensitivity of seven commercial SARS CoV-2 antibody tests.

2.1. Serum samples

Blood specimens were obtained from adult individuals with positive SARS CoV-2 RNA test after informed consent. Selected participants had mild to moderate symptoms or were asymptomatic (Table S1). Ex post, four viral RNA-positive participants that were asymptomatic and were tested as part of routine screening for health care workers or before surgery without contact with infected persons were excluded. This led to seventy-three sera from 57 patients for the antibody test evaluation. Sixteen individuals gave blood at two times points. Sera were obtained between 2 and 10 weeks after viral RNA testing. Sera were frozen at −20 °C until testing. During the study, serum samples were thawed 1–4 times.

2.2. Commercial antibody tests

Sera were tested with the following SARS-CoV-2 antibody tests: Roche Elecsys Anti-SARS-CoV-2, Abbott Architect SARS-CoV-2 IgG, Novatec Novalisa SARS-CoV-2 IgG ELISA, Virotech SARS-CoV-2 IgG ELISA, Euroimmun Anti-SARS-CoV-2-ELISA (IgG), Mediagnost Anti-SARS CoV-2 ELISA, and Siemens Atellica IM COV2T. The antibody tests from Abbott, Roche, Novatec and Virotech measure SARS CoV-2 nucleoprotein-specific antibodies. The tests from Siemens, Euroimmun and Mediagnost detect antibodies against the glycoprotein S1 or the receptor binding site of S1. The tests from Abbott, Novatec, Virotech, Euroimmun and Mediagnost were specific for IgG. The ECLIA from Roche and the MIA from Siemens are antigen-bridging assays that measure several immunoglobulin classes simultaneously.

The Roche test was performed with an automated Cobas e 601 analyzer, the Abbott test was performed with the ARCHITECT i system, the Euroimmun ELISAs were performed with an automated ELISA processor (DSX, Dynex Technologies, U. K.). The Siemens test was performed with the Atellica IM Analizer, the Novatec, Virotech and Mediagnost ELISAs were performed manually. According to the manufacturers, the tests had sensitivities between 86.3 and 100 % and specificities from 97 to 100 %. The tests were performed in three diagnostic routine laboratories and a research laboratory according to the instructions of the manufacturers. Table S2 shows a comparison of the technical procedure of the tests and the test characteristics according to the information from the manufacturers.

2.3. Data analysis

For the calculation of test sensitivity, borderline results were regarded as negative. Data were arranged in tables and calculations were made with Microsoft Excel software. The 95 % confidence intervals were determined using the Medcalc “Test for one proportion” calculator based on the Clopper-Pearson confidence interval. Proportions were compared using the Medcalc “Comparison of proportions” calculator that uses the N-1 Chi-squared test (https://www.medcalc.org/calc/comparison_of_proportions.php).

3. Results

3.1. Positive rate and concordance of the antibody tests

The antibody tests reacted with varying numbers of sera. Tests were positive with 13–20 of the 25 sera (52.0–80.0 %) obtained 2 − 3 weeks after positive RNA test and with 32–48 of 48 sera (66.7–100 %) obtained 4–10 weeks after viral RNA testing. The overall rate of positive tests ranged from 64.4–93.2%. Nucleoprotein-based antibody tests showed between 65.8 and 90.4 % positive results. Glycoprotein-based assays recognized 64.4–93.2% of the sera (Table 1).

The Roche and the Siemens tests were more sensitive with sera obtained 4–10 weeks after the RNA test than with sera obtained earlier. Numerically, the Siemens test had the highest positive rate. Statistically, the sensitivity of the Siemens, Roche and Euroimmun assays was indistinguishable. The sensitivity of the Abbott test was slightly lower than the Siemens test, comparable with the Roche and Euroimmun assays, and higher than the Novatec, Virotech and Mediagnost ELISAs. The sensitivity of the Novatec, Virotech and Mediagnost ELISAs was comparable and lower than that of the other tests (Table 2). The concordance of the tests ranged from 67.1–94.5%. The largest concordance was between the Roche and the Siemens assays that recognize antibodies against different viral proteins (94.5 %, Table 3).

3.2. Breakdown of test results

Breakdown analysis of the test results showed that nucleoprotein and glycoprotein-based tests reacted with different sets of sera. For example, among the sera obtained 4–10 weeks after the RNA test, six of the 8 negative sera in the nucleoprotein-based Abbott test were positive in the glycoprotein-based Euroimmun test. Similarly, 6 of the 14 negative or borderline sera of the Mediagnost ELISA were positive in the Novatec assay. Two sera (CV220/027 − 1 and CoV-036) that were negative in all nucleoprotein antibody tests were positive in the glycoprotein-based tests.

In contrast, the nucleoprotein- or the glycoprotein-based tests as groups showed an association of sensitivity and the pattern of positive and negative results. Sera that were negative in tests with higher reactivity were usually also negative in tests with lower reactivity. For instance, the two sera that were negative in the Roche test were also negative in the Abbott test. Seven of 8 sera that were negative in the Abbott test were also negative in the Novatec ELISA. All 5 sera that were negative in the Euroimmun ELISA were also negative in the Mediagnost ELISA (Table 4).

4. Discussion

The study examined the sensitivity of seven SARS CoV-2 antibody tests for the laboratory and compared the reactivity pattern of the tests in a prospective study. The serum samples were from patients with positive SARS CoV-2 RNA tests. Most of the participants had mild to moderate disease. Some were asymptomatic and none of them was seriously ill or required hospital care. Sera from routine viral RNA testing before surgery or from screening of health care workers without relevant contact were excluded because they were considered of lower pretest probability of infection posing a risk of false-positive RNA results. Sera were divided into groups obtained 2 − 3 and 4–10 weeks after the RNA tests. Sera from symptomatic participants fell into the same groups when classified according to the day of symptom onset.

Studies about the antibody response in SARS patients from 2002/2003 showed significant differences between the antibody response to the nucleoprotein and the glycoprotein. Nucleoprotein-specific antibody responses were detected in 89–94 % of sera whereas glycoprotein-specific responses were found in only 59–63 % of the sera [5,6]. This suggested that antibody assays based on the nucleoprotein might be more sensitive than those based on the glycoprotein. The results of this study show that for Covid-19, antibody tests based on the viral nucleoprotein and the glycoprotein have comparable sensitivity. It generally confirms the specifications of the test manufacturers and the results of a previous study [2].

The sensitivity of the Siemens and Roche tests was significantly higher with sera obtained 4–10 weeks after viral RNA test. A trend towards higher sensitivity at later time points was also seen with the Euroimmun and the Mediagnost test. Thus, antibody testing 2 − 3 weeks after symptom onset or RNA testing is less reliable than testing 4 weeks after diagnosis.

The Siemens antibody test was the most sensitive test followed by

Table 1
Sensitivity of SARS CoV-2 IgG and total antibody tests (Roche, Siemens) with sera obtained 2-3 and > 4 weeks after viral RNA testing.

Blood drawing	No. of sera	Roche % Sensitivity [95 % confidence interval]*	Abbott	Novatec	Virotech	Siemens	Euroimmun	Mediagnost
2 − 3 weeks	25	**80.0**** [59.3; 93.2]	**80.0** [59.3; 93.2]	**72.0** [50.6; 87.9]	**64.0** [42.5; 82.0]	**80.0***** [59.3; 93.2]	**72.0** [50.6; 87.9]	**52.0** [31.3; 72.2]
≥ 4 weeks	48	**95.8**** [85.7; 99.5]	**83.3** [69.7; 92.5]	**66.7** [51.6; 79.6]	**66.7** [51.6; 79.6]	**100***** [92.8; 100]	**89.6** [77.4; 96.5]	**70.8** [55.9; 83.0]
in total	73	**90.4** [81.2; 96.1]	**82.2** [71.5; 90.2]	**68.5** [56.6; 78.9]	**65.8** [53.8; 76.5]	**93.2** [84.8; 97.8]	**83.6** [73.1; 91.2]	**64.4** [52.3; 75.3]

* For calculations, borderline results were considered negative.
** The sensitivity of the test differs significantly (p = 0.0309) between the period of 2 − 3 weeks and the period of 4 weeks or longer.
*** The sensitivity of the test differs significantly (p = 0.0014) between the period of 2 − 3 weeks and the period of 4 weeks or longer.

Table 2
Significance level (p-value) for comparison of the sensitivity of the tests.

Test	Roche	Abbott	Novatec	Virotech	Siemens	Euroimmun	Mediagnost
Roche	x	0.1511	0.0011*	0.0003*	0.5389	0.2235	0.0002*
Abbott		x	0.0556	0.0244*	0.0437*	0.8229	0.0154*
Novatec			x	0.7293	0.0002*	0.0332*	0.6011
Virotech				x	< 0.0001*	0.0137*	0.8596
Siemens					x	0.0711	< 0.0001*
Euroimmun						x	0.0084*

* The reactivity differs significantly between the two assays (p < 0.05).

Table 3
Level of concordance of antibody tests in %.

Test	Roche	Abbott	Novatec	Virotech	Siemens	Euroimmun	Mediagnost
Roche	x	89.0	72.6	75.3	94.5	87.7	68.5
Abbott		x	80.82	83.6	83.6	82.2	74.0
Novatec			x	91.8	67.1	71.2	71.2
Virotech				x	69.9	74.0	74.0
Siemens					x	87.7	68.5
Euroimmun						x	80.8

the Roche, Euroimmun and Abbott tests. The high sensitivity of the antigen-bridging tests from Roche and Siemens could be due to the ability of the tests to detect all immunoglobulin classes. The Novatec, Virotech and Mediagnost assays were less sensitive. The sensitivity of the Siemens, Roche and Euroimmun tests were in the 95 % confidence interval of the sensitivity specified by the manufacturers and reported previously by others [7–9]. The Abbott, Novatec, Virotech and Mediagnost ELISAs test were slightly less sensitive than specified by the manufacturers.

Sensitivity values of the antibody tests are of high relevance for the interpretation of seroepidemiologic studies. Antibody tests are already being used for SARS CoV-2 seroprevalence studies [10]. The sensitivity of SARS CoV-2 antibody tests interferes with serosurveillance in a complex scheme. At low prevalence, small deviations from a sensitivity of 100 % improve the results. For instance, at a true seroprevalence of 2% and a test specificity of 99.5 %, an antibody assay with a sensitivity of 100 % gives an erroneously slightly elevated prevalence of 2.5 % because of 0.5 % false positive results. A test with a sensitivity of 75 % gives the correct 2.0 %, because of 0.5 % (25 % of 2%) false negative results that balance the false positive results. Lower test sensitivity than 75 % leads to falsely lower values. At increasing true prevalence of the disease, similar deviations of the sensitivity have a more visible effect. For instance, at a true prevalence of 20 %, a test with a specificity of 99.5 % and a sensitivity of 100 % indicates a prevalence of 20.4 % and a test with a sensitivity of 75 % shows 15.4 %. Thus, test sensitivity values obtained in this and similar studies help to exactly determine the SARS CoV-2 seroprevalence.

The observation that negative sera in nucleoprotein- and glycoprotein-based antibody tests differed indicates that combining nucleoprotein- and glycoprotein-based tests increases the number of positive results. In our sample, 14 of 48 sera obtained > 4 weeks after RNA testing, were negative in the glycoprotein-based Mediagnost test. Retesting of the 14 sera with the Novatec ELISA would have identified 6 more positive sera, increasing the positive rate from 70.8%–83.3%. This is not being observed when combining two of the nucleoprotein- or glycoprotein-based assays. When two antibody tests based on the same antigen are being used, the positive rate is similar or identical to that of the more sensitive assay. This indicates that a combination of nucleoprotein- and glycoprotein-based ELISAs would increase the number of true positives. From a clinical perspective, a sequential test algorithm must be considered carefully, because it increases cost and labor.

The study was limited by the number of sera examined. This led to relatively broad 95 % confidence intervals of the sensitivity. For refinement of the sensitivity values, a larger number of sera must be tested. The study did not assess the specificity of the assays because of the unsuitable study cohort for answering this question and the large number of additional tests needed for informative specificity analyses. The test manufacturers determined the specificity of their tests with several hundreds to thousands of negative sera. Similar numbers of specimens likely have to be tested to evaluate the specificity indicated by the manufacturers.

In conclusion, nucleoprotein- and glycoprotein-based SARS CoV-2 antibody tests had a similar range of sensitivities. The most sensitive assays recognized 95.8–100 % of sera if the sera were taken at least 4 weeks after RNA testing. Sequential testing with nucleoprotein- and glycoprotein-based ELISAs increases the positive rate and is most useful when highly sensitive antibody tests are not available. The sensitivity values of the tests are useful for calculating the frequency of SARS CoV-2 exposure in seroprevalence studies.

Table 4
Comparison of the reactivity of SARS CoV-2 antibody tests with individual sera.

		Roche		Abbott		Novatec		Virotech		Siemens		Euroimmun		Mediagnost	
	Sample	Result	N - COI	Result	N - Index	Result	N - NTU	Result	N - VE	Result	S - Index	Result	S - Ratio	Result	S - OD
2-3 weeks (N=25)	CV220/013-1	+	11.7	+	4.9	+	13.9	+	16.1	-	0.51	+	1.4	+	0.90
	CV220/001-1	+	49.3	+	7.0	+	26.5	+	30.4	+	> 10	+	5.3	+	2.22
	CV220/006-1	+	60.5	+	8.9	+	25.3	+	29.5	+	> 10	+	4.7	+	2.49
	CV220/010-1	+	26.3	+	5.0	+	25.0	+	31.8	+	> 10	+	7.0	+	2.95
	CV220/011-1	+	20.8	+	6.8	+	14.2	+	19.6	+	4.29	+	3.0	+	1.45
	CV220/035-1	+	78.1	+	7.6	+	21.1	+	29.6	+	6.71	+	2.1	+	1.33
	CoV-001	+	25.4	+	7.0	+	18.7	+	17.4	+	> 10	+	4.9	+	2.33
	CoV-013	+	49.9	+	8.7	+	27.8	+	33.9	+	> 10	+	8.9	+	2.90
	CoV-016	+	47.7	+	7.0	+	29.0	+	26.3	+	> 10	+	7.9	+	2.56
	CoV-025	+	26.0	+	6.4	+	15.2	+	17.2	+	3.07	+	1.9	+	0.69
	CoV-035	+	92.1	+	9.3	+	21.5	+	26.2	+	> 10	+	3.6	+	1.46
	CoV-042	+	53.7	+	6.7	+	17.7	+	24.8	+	7.77	+	5.4	+	1.94
	CV220/002-1	+	3.2	+	3.8	+	11.0	+	11.7	+	1.5	+	1.1	+/-	0.59
	CV220/024-1	+	17.0	+	4.3	+	12.3	+	16.3	+	5.85	+	1.7	+/-	0.83
	CV220/026-1	+	2.3	+	1.8	+	12.3	+	13.1	+	1.81	+	1.4	+/-	0.54
	CV220/039-1	+	22.7	+	5.6	+	13.1	+	16.7	+	2.21	-	0.8	-	0.30
	CV220/008-1	+	4.0	+	3.7	+/-	10.0	+/-	10.6	+	2.06	+	1.6	+/-	0.70
	CV220/012-1	+	1.1	+	2.6	+/-	10.6	-	6.0	+	1.98	+/-	0.9	-	0.43
	CV220/003-1	+	2.4	+	3.1	-	5.9	-	8.9	+	2.4	+	1.2	-	0.31
	CoV-034	+	8.4	-	0.76	-	3.1	-	3.9	+	5.35	+/-	1.0	+/-	0.41
	CV220/021-1	-	0.4	+	1.5	+	11.8	-	8.3	-	0.7	-	0.7	-	0.37
	CoV-041	-	0.6	-	1.2	+	12.8	+/-	9.9	-	0.65	+/-	0.9	-	0.34
	CV220/027-1	-	0.7	-	1.1	-	7.0	-	5.6	+	4.53	+	2.2	+	1.21
	CV220/022-1	-	0.5	-	1.3	-	5.3	-	1.7	-	0.5	-	0.7	-	0.10
	CoV-009	-	0.1	-	0.1	-	6.3	-	1.1	-	< 0.05	-	0.2	-	0.09
≥ 4 weeks (N=48)	CV220/002-2	+	28.3	+	3.6	+	12.5	+	15.7	+	5.93	+	3.1	+	1.09
	CV220/008-2	+	90.4	+	3.9	+	15.3	+	19.1	+	> 10	+	5.3	+	1.77
	CV220/012-2	+	15.3	+	5.1	+	18.5	+	19.7	+	> 10	+	6.2	+	1.67
	CV220/001-2	+	88.4	+	7.7	+	25.5	+	31.4	+	> 10	+	7.5	+	1.85
	CV220/006-2	+	87.9	+	8.8	+	23.8	+	29.5	+	> 10	+	9.7	+	2.35
	CV220/010-2	+	75.5	+	7.0	+	24.6	+	33.6	+	> 10	+	11.1	+	2.93
	CV220/011-2	+	63.6	+	6.5	+	15.7	+	21.0	+	> 10	+	6.2	+	1.91
	CV220/024-2	+	87.0	+	5.1	+	13.8	+	18.6	+	> 10	+	4.4	+	1.54
	CV220/035-2	+	108.5	+	7.5	+	18.5	+	32.8	+	> 10	+	4.4	+	1.58
	CoV-002	+	65.8	+	6.0	+	16.4	+	18.6	+	> 10	+	6.8	+	2.28
	CoV-003	+	105.8	+	6.0	+	24.7	+	29.2	+	> 10	+	6.0	+	2.26
	CoV-004	+	128.0	+	6.9	+	28.8	+	41.0	+	> 10	+	5.4	+	2.19
	CoV-006	+	153.5	+	7.8	+	21.0	+	24.7	+	> 10	+	6.2	+	2.27
	CoV-014	+	53.6	+	3.5	+	18.6	+	18.6	+	> 10	+	3.8	+	1.46
	CoV-015	+	27.6	+	3.4	+	11.8	+	12.6	+	5.73	+	1.9	+	0.83
	CoV-021	+	29.2	+	5.9	+	20.2	+	18.5	+	> 10	+	7.0	+	2.14
	CoV-022	+	114.6	+	7.2	+	26.2	+	31.4	+	> 10	+	3.2	+	1.37
	CoV-023	+	108.7	+	5.0	+	16.4	+	17.1	+	> 10	+	4.4	+	1.86
	CoV-026	+	28.7	+	4.2	+	20.8	+	21.1	+	> 10	+	7.4	+	2.59
	CoV-028	+	26.3	+	3.9	+	19.4	+	14.4	+	7.53	+	2.4	+	0.82
	CoV-029	+	109.0	+	7.3	+	24.0	+	31.2	+	9.38	+	2.5	+	0.94
	CoV-030	+	87.6	+	7.5	+	19.2	+	22.9	+	> 10	+	8.0	+	2.63
	CoV-032	+	52.5	+	4.5	+	12.1	+	17.9	+	> 10	+	5.1	+	1.64
	CoV-038	+	66.8	+	3.5	+	11.4	+	11.2	+	> 10	+	3.3	+	1.00
	CoV-045	+	41.2	+	4.5	+	29.4	+	39.4	+	> 10	+	7.6	+	2.53
	CoV-027	+	81.9	+	6.7	+	24.3	+	29.5	+	3.87	+	1.5	+/-	0.63
	CV220/039-2	+	43.3	+	5.4	+	13.8	+	17.8	+	2.5	+	1.2	+/-	0.61
	CV220/013-2	+	36.5	+	5.9	+	17.5	+	22.4	+	1.83	+	2.5	+/-	0.82
	CoV-012	+	57.9	+	5.6	+	16.6	+	16.4	+	1.83	-	0.8	+/-	0.41
	CoV-020	+	108.1	+	7.4	+	18.6	+	21.2	+	1.13	-	0.7	-	0.36
	CoV-039	+	92.2	+	3.0	+	12.7	+/-	10.3	+	> 10	+	4.7	+	1.32
	CV220/026-2	+	14.9	+	1.4	+/-	11.0	+	11.7	+	4.68	+	2.8	+/-	0.57
	CoV-031	+	25.8	+	4.9	+/-	9.6	+	13.0	+	6.89	+	2.3	+	0.91
	CoV-019	+	23.3	+	2.6	+/-	9.9	+/-	9.5	+	> 10	+	3.6	+	1.23
	CoV-005	+	39.7	+	3.1	+/-	10.5	+/-	10.2	+	> 10	+	4.0	+	1.53
	CoV-024	+	22.4	+	1.8	+/-	9.6	-	8.2	+	9.62	+	5.2	+	2.07
	CoV-043	+	6.6	+	2.8	-	8.1	-	6.6	+	8.27	+	1.6	+/-	0.56
	CoV-044	+	3.8	+	2.2	-	8.5	-	3.4	+	3.74	+/-	0.9	+/-	0.66
	CoV-017	+	33.0	+	1.4	-	6.8	-	4.6	+	6.62	+	1.3	+	0.75
	CoV-018	+	51.0	+	2.8	-	6.8	-	7.7	+	> 10	+	2.2	+	0.82
	CV220/021-2	+	3.5	-	1.2	+	11.3	-	8.0	+	4.5	+	1.3	+/-	0.67
	CoV-040	+	1.6	-	0.3	+/-	9.5	-	3.7	+	1.91	-	0.8	-	0.35
	CoV-033	+	3.3	-	1.2	-	8.6	-	8.9	+	2.74	+	1.4	+/-	0.48
	CV220/027-2	+	5.0	-	0.9	-	6.9	-	5.6	+	> 10	+	5.4	+	1.44
	CV220/022-2	+	1.8	-	1.3	-	5.3	-	5.4	+	1.56	+	1.6	-	0.32
	CV220/003-2	+	5.1	-	1.3	-	4.4	-	6.1	+	3.06	+	1.5	-	0.38
	CoV-036	-	0.7	-	1.0	-	8.3	-	4.9	+	7.93	+	3.2	+	1.49
	CoV-011	-	0.3	-	0.3	-	8.0	-	2.3	+	4.81	-	0.8	+/-	0.51

CRediT authorship contribution statement

Carolin Schnurra: Methodology, Formal analysis, Investigation, Writing - review & editing. **Nina Reiners:** Investigation, Writing - review & editing. **Ronald Biemann:** Investigation, Writing - review & editing. **Thorsten Kaiser:** Methodology, Writing - review & editing. **Henning Trawinski:** Methodology, Resources, Writing - review & editing. **Christian Jassoy:** Conceptualization, Methodology, Formal analysis, Writing - review & editing.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2020.104544.

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