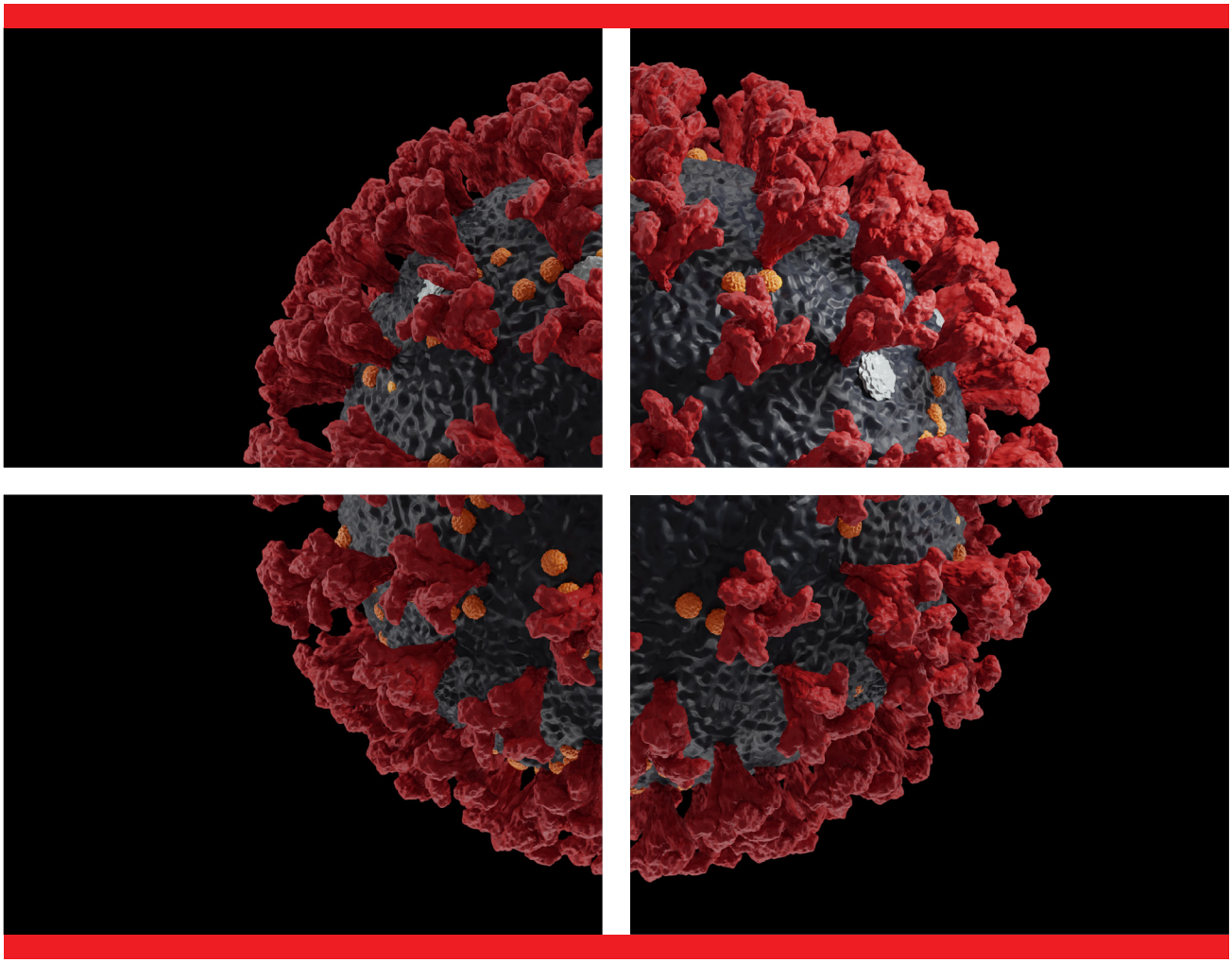
Publication List
COVID-19: SARS-CoV-2 Ab ELISA



Human
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Disclaimer

*This document contains a selection of relevant scientific publications related to COVID-19, some of which are not yet peer-reviewed (marked with *).*

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Content

Performance of the SARS-CoV-2 Ab ELISA

Towards the next phase: evaluation of serological assays for diagnostics and exposure assessment

Corine H. GeurtsvanKessel, Nisreen M.A. Okba, Zsofia Igloi, Carmen W.E. Embregts, Brigitta M. Laksono, Lonneke Leijten, Janette Rahamat-Langendoen, Johannes P.C. van den Akker, Jeroen J.A. van Kampen, Annemiek A. van der Eijk, Rob S. van Binnendijk, Bart Haagmans, Marion Koopmans
– medRxiv; https://doi.org/10.1101/2020.04.23.20077156 –

Abstract

The world is entering a new era of the COVID-19 pandemic in which there is an increasing call for reliable antibody testing. To support decision making on the deployment of serology for either population screening or diagnostics, we present a comprehensive comparison of serological COVID-19 assays. We show that the assay detecting total immunoglobulins against the receptor binding domain of SARS CoV-2, had optimal characteristics for antibody detection in different stages of disease.

Evaluation of nine commercial SARS-CoV-2 immunoassays

Ria Lassaunière, Anders Frische, Zitta B. Harboe, Alex C.Y. Nielsen, Anders Fomsgaard, Karen A. Krogfelt, Charlotte S. Jørgensen
– medRxiv; https://doi.org/10.1101/2020.04.09.20056325 –

Abstract

Due to urgency and demand, numerous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoassays are rapidly being developed and placed on the market with limited validation on clinical samples. Thorough validation of serological tests are required to facilitate their use in the accurate diagnosis of SARS-CoV-2 infection, confirmation of molecular results, contact tracing, and epidemiological studies. This study evaluated the sensitivity and specificity of nine commercially available serological tests. These included three enzyme-linked immunosorbent assays (ELISAs) and six point-of-care (POC) lateral flow tests. The assays were validated using serum samples from: i) SARS-CoV-2 PCR-positive patients with a documented first day of disease; ii) archived sera obtained from healthy individuals before the emergence of SARS-CoV-2 in China; iii) sera from patients with acute viral respiratory tract infections caused by other coronaviruses or non-coronaviruses; and iv) sera from patients positive for dengue virus, cytomegalovirus and Epstein Barr virus. The results showed 100% specificity for the Wantai SARS-CoV-2 Total Antibody ELISA, 93% for the Euroimmun IgA ELISA, and 96% for the Euroimmun IgG ELISA with sensitivities of 90%, 90%, and 65%, respectively. The overall performance of the POC tests according to manufacturer were in the rank order of AutoBio Diagnostics > Dynamiker Biotechnology = CTK Biotech > Artron Laboratories > Acro Biotech ≥ Hangzhou Alltest Biotech. Overall, these findings will facilitate selection of serological assays for the detection SARS-CoV-2-specific antibodies towards diagnosis as well as sero-epidemiological and vaccine development studies.

Kinetics of the humoral immune response to SARS-CoV-2: comparative analytical performance of seven commercial serology tests

Pauline H. Herroelen, Geert A. Martens, Dieter De Smet, Koen Swaerts, An-Sofie Decavele

– medRxiv; https://doi.org/10.1101/2020.06.09.20124719 –

Abstract

Background

SARS-CoV-2 serology tests are clinically useful to document a prior SARS-CoV-2 infection in patients with no or inconclusive PCR results and suspected COVID-19 disease or sequelae. Data are urgently needed to select the assays with optimal sensitivity at acceptable specificity.

Methods

A comparative analysis of analytical sensitivity was performed of seven commercial SARS-CoV-2 serology assays on 171 sera from 135 subjects with PCR-confirmed SARS-CoV-2 infection, composed of 71 patients hospitalized for COVID-19 pneumonia and 64 healthcare workers with paucisymptomatic infections. The kinetics of IgA/IgM/IgG seroconversion to viral N- and S-protein epitopes were studied from 0 to 54 days after symptom onset. Specificity was verified on 57 pre-pandemic samples.

Results

Wantai SARS-COV-2 Ab ELISA and Orient Gene COVID-19 IgG/IgM Rapid Test achieved a superior overall sensitivity. Elecsys Anti-SARS-CoV-2 and EUROIMMUN Anti-SARS-CoV-2 combined IgA/IgG also showed acceptable sensitivity (>95%) versus the consensus result of all assays from 10 days post symptom onset. Optimal specificity (>98%) was achieved only by Wantai SARS-COV-2 Ab ELISA, Elecsys Anti-SARS-CoV-2 assay and Innovita 2019-nCoV Ab rapid test. LIAISON SARS-CoV-2 S1/S2 IgG showed a significantly lower sensitivity as compared to all other assays. Lack of seroconversion by any test was seen in 1.4% of hospitalized and 4.7% of paucisymptomatic infections. Within 10 days from symptom onset, only the Wantai SARS-COV-2 Ab ELISA showed acceptable sensitivity.

Conclusions

Wantai SARS-COV-2 Ab ELISA and Elecsys Anti-SARS-CoV-2 assays are suitable for sensitive and specific screening of a SARS-CoV-2 infection from 10 days after symptom onset.

Diagnostic performances and thresholds: the key to harmonization in serological SARS-CoV-2 assays?

Mario Plebani, Andrea Padoan, Davide Negrini, Benedetta Carpinteri, Laura Sciacovelli
– medRxiv; https://doi.org/10.1101/2020.05.22.20106328–

Abstract

Background

The evaluation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) specific antibody (Ab) assay performances is of the utmost importance in establishing and monitoring virus spread in the community. In this study focusing on IgG antibodies, we compare reliability of three chemiluminescent (CLIA) and two enzyme linked immunosorbent (ELISA) assays.

Methods

Sera from a total of 271 subjects, including 64 reverse transcription-polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 patients were tested for specific Ab using Maglumi (Snibe), Liaison (Diasorin), iFlash (Yhlo), Euroimmun (Medizinische Labordiagnostika AG) and Wantai (Wantai Biological Pharmacy) assays. Diagnostic sensitivity and specificity, positive and negative likelihood ratios were evaluated using manufacturers' and optimized thresholds.

Results

Optimized thresholds (Maglumi 2 kAU/L, Liaison 6.2 kAU/L and iFlash 15.0 kAU/L) allowed us to achieve a negative likelihood ratio and an accuracy of: 0.06 and 93.5% for Maglumi; 0.03 and 93.1% for Liaison; 0.03 and 91% for iFlash. Diagnostic sensitivities and specificities were above 93.8% and 85.9%, respectively for all CLIA assays. Overall agreement was 90.3% (Cohen's kappa = 0.805 and SE = 0.041) for CLIA, and 98.4% (Cohen's kappa = 0.962 and SE = 0.126) for ELISA.

Conclusions

The results obtained indicate that, for CLIA assays, it might be possible to define thresholds that improve the negative likelihood ratio. Thus, a negative test result enables the identification of subjects at risk of being infected, who should then be closely monitored over time with a view to preventing further viral spread. Redefined thresholds, in addition, improved the overall inter-assay agreement, paving the way to a better harmonization of serologic tests.

Performance of SARS-CoV-2 antibody assays in different stages of the infection: Comparison of commercial ELISA and rapid tests

Traugott M., Aberle SW., Aberle JH., Griebler H., Karolyi M., Pawelka E., Puchhammer-Stöckl E., Zoufaly A., Weseslindtner L.

– The Journal of Infectious Diseases, jiaa305, https://doi.org/10.1093/infdis/jiaa305 –

Abstract

We comparatively assessed sensitivities and specificities of 4 commercial enzyme-linked immunosorbent assays (ELISAs) and 2 rapid tests in 77 patients with polymerase chain reaction–confirmed severe acute respiratory syndrome coronavirus 2 infection, grouped by interval since symptom onset. Although test sensitivities were low (<40%) within the first 5 days after disease onset, immunoglobulin (Ig) M, IgA, and total antibody ELISAs increased in sensitivity to >80% between days 6 and 10 after symptom onset. The evaluated tests (including IgG and rapid tests) provided positive results in all patients at or after the 11th day after onset of disease. The specificities of the ELISAs were 83% (IgA), 98% (IgG), and 97% (IgM and total antibody).

Herd immunity is not a realistic exit strategy during a COVID-19 outbreak

Ed Slot, Boris M. Hogema, Chantal B.E.M. Reusken, Johan H. Reimerink, Michel Molier, Jan H.M. Karregat, Johan IJlst, Věra M.J. Novotný, René A.W. van Lier, Hans L. Zaaijer

– doi: 10.21203/rs.3.rs-25862/v1–

Abstract

The world is combating an ongoing COVID-19 pandemic1-4. Health-care systems, society and the economy are impacted in an unprecedented way. It is unclear how many people have contracted the causative coronavirus (SARS-CoV-2) unknowingly. Therefore, reported COVID-19 cases do not reflect the true scale of outbreak5-9. Natural herd immunity has been suggested as a potential exit strategy during COVID-19 outbreaks, which may arise when 50-67% of a community has been infected10. Here we present the prevalence and distribution of antibodies to SARS-CoV-2 in a healthy adult population of a highly affected country using a novel immunoassay, indicating that one month into the outbreak (i) the seroprevalence in the Netherlands is 2.7% with substantial regional variation, (ii) the hardest-hit areas show a seroprevalence of up to 9.5%, (iii) the seroprevalence is sex-independent throughout age groups (18-72 years), (iv) antibodies are significantly more often detected in younger people (18-30 years), and (v) the number of immune individuals in the current epidemic stage is far below the herd immunity threshold. This study provides vital information on the extent of virus spread in a country where social distancing is in place, concluding that herd immunity to SARS-CoV-2 is not a realistic short-term exit strategy option.

Comparison of diagnostic accuracies of rapid serological tests and ELISA to molecular diagnostics in patients with suspected coronavirus disease 2019 presenting to the hospital

D.S.Y. Ong, S.J. de Man, F.A. Lindeboom, J.G.M. Koeleman

– Clinical Microbiology and Infection; https://doi.org/10.1016/j.cmi.2020.05.028 –

Abstract

Background

To assess the diagnostic performance of rapid lateral flow immunochromatographic assays (LFAs) compared with an ELISA and nucleic acid amplification tests (NATs) in individuals with suspected coronavirus disease 2019 (COVID-19).

Methods

Patients presenting to a Dutch teaching hospital were eligible between 17 March and 10 April 2020, when they had respiratory symptoms that were suspected for COVID-19. The performances of six different LFAs were evaluated in plasma samples obtained on corresponding respiratory sample dates of NATs testing. Subsequently, the best performing LFA was evaluated in 228 patients and in 50 sera of a historical patient control group.

Results

In the pilot analysis, sensitivity characteristics of LFA were heterogeneous, ranging from 2/20 (10%; 95% CI 0%–23%) to 11/20 (55%; 95% CI 33%–77%). In the total cohort, Orient Gene Biotech COVID-19 IgG/IgM Rapid Test LFA had a sensitivity of 43/99 (43%; 95% CI 34%–53%) and specificity of 126/129 (98%; 95% CI 95%–100%). Sensitivity increased to 31/52 (60%; 95% CI 46%–73%) in patients with at least 7 days of symptoms, and to 21/33 (64%; 95% CI 47%–80%) in patients with C-reactive protein (CRP) ≥100 mg/L. Sensitivity and specificity of Wantai SARS-CoV-2 Ab ELISA was 59/95 (62%; 95% CI 52%–72%) and 125/128 (98%; 95% CI 95%–100%) in all patients, respectively, but sensitivity increased to 38/48 (79%; 95% CI 68%–91%) in patients with at least 7 days of symptoms.

Conclusions

There is large variability in diagnostic test performance between rapid LFAs, but overall limited sensitivity and high specificity in acutely admitted patients. Sensitivity improved in patients with longer existing symptoms or high CRP. LFAs should only be considered as additional triage tools when these may lead to the improvement of hospital logistics.

Antibody response in COVID-19 patients

Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019

Yujiao Jina, Miaochan Wanga, Zhongbao Zuoa, Chaoming Fanb, Fei Yec, Zhaobin Caid, Ying Wanga, Huaizhong Cuia, Kenu Pana, Aifang Xua

– *International Journal of Infectious Diseases 94 (2020) 49–52; https://doi.org/10.1016/j.ijid.2020.03.065–*

Abstract

Background

To investigate the diagnostic value of serological testing and dynamic variance of serum antibody in coronavirus disease 2019 (COVID-19).

Methods

This study retrospectively included 43 patients with a laboratory-confirmed infection and 33 patients with a suspected infection, in whom the disease was eventually excluded. The IgM/IgG titer of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was measured by chemiluminescence immunoassay analysis.

Results

Compared to molecular detection, the sensitivities of serum IgM and IgG antibodies to diagnose COVID-19 were 48.1% and 88.9%, and the specificities were 100% and 90.9%, respectively.In the COVID-19 group, the IgM-positive rate increased slightly at first and then decreased over time; in contrast, the IgG-positive rate increased to 100% and was higher than IgM at all times. The IgM-positive rate and titer were not significantly different before and after conversion to virus-negative. The IgG-positive rate was up to 90% and not significantly different before and after conversion to virus-negative. However, the median IgG titer after conversion to virus-negative was double that before, and the difference was significant.

Conclusions

Viral serological testing is an effective means of diagnosis for SARS-CoV-2 infection. The positive rate and titer variance of IgG are higher than those of IgM in COVID-19.

Antibody responses to SARS-CoV-2 in patients with COVID-19

Quan-Xin Long, Bai-Zhong Liu, Hai-Jun Deng, Gui-Cheng Wu, Kun Deng, Yao-Kai Chen, Pu Liao, Jing-Fu Qiu, Yong Lin, Xue-Fei Cai, De-Qiang Wang, Yuan Hu, Ji-Hua Ren, Ni Tang, Yin-Yin Xu, Li-Hua Yu, Zhan Mo, Fang Gong, Xiao-Li Zhang, Wen-Guang Tian, Li Hu, Xian-Xiang Zhang, Jiang-Lin Xiang, Hong-Xin Du, Hua-Wen Liu, Chun-Hui Lang, Xiao-He Luo, Shao-Bo Wu, Xiao-Ping Cui, Zheng Zhou, Man-Man Zhu, Jing Wang, Cheng-Jun Xue, Xiao-Feng Li, Li Wang, Zhi-Jie Li, Kun Wang, Chang-Chun Niu, Qing-Jun Yang, Xiao-Jun Tang, Yong Zhang, Xia-Mao Liu, Jin-Jing Li, De-Chun Zhang, Fan Zhang, Ping Liu, Jun Yuan, Qin Li, Jie-Li Hu, Juan Chen, Ai-Long Huang

– Nat Med 26, 845–848 (2020). https://doi.org/10.1038/s41591-020-0897-1 –

Abstract

We report acute antibody responses to SARS-CoV-2 in 285 patients with COVID-19. Within 19 days after symptom onset, 100% of patients tested positive for antiviral immunoglobulin-G (IgG). Seroconversion for IgG and IgM occurred simultaneously or sequentially. Both IgG and IgM titers plateaued within 6 days after seroconversion. Serological testing may be helpful for the diagnosis of suspected patients with negative RT–PCR results and for the identification of asymptomatic infections.

Interpreting Diagnostic Tests for SARS-CoV-2

Nandini Sethuraman, Sundararaj Stanleyraj Jeremiah, Akihide Ryo

– JAMA. 2020;323(22):2249-2251. doi:10.1001/jama.2020.8259 –

Abstract

The pandemic of coronavirus disease 2019 (COVID-19) continues to affect much of the world. Knowledge of diagnostic tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still evolving, and a clear understanding of the nature of the tests and interpretation of their findings is important. This Viewpoint describes how to interpret 2 types of diagnostic tests commonly in use for SARS-CoV-2 infections—reverse transcriptase–polymerase chain reaction (RT-PCR) and IgM and IgG enzyme-linked immunosorbent assay (ELISA)—and how the results may vary over time.

COVID-19 and Postinfection Immunity

Robert D. Kirkcaldy, Brian A. King, John T. Brooks

– *JAMA. 2020;323(22):2245-2246. doi:10.1001/jama.2020.7869* –

Abstract

In the absence of effective treatment or biomedical prevention, efforts to control the coronavirus disease 2019 (COVID-19) pandemic have relied on nonpharmaceutical interventions such as personal preventive actions (eg, handwashing, face covers), environmental cleaning, physical distancing, stay-at-home orders, school and venue closures, and workplace restrictions adopted at the national, state, and local levels. In addition to these public health interventions, development of herd immunity could also provide a defense against COVID-19. However, whether immunity occurs among individuals after they have recovered from COVID-19 is uncertain. Many human infections with other viral pathogens, such as influenza virus, do not produce a durable immune response.

Differences in antibody kinetics and functionality between severe and mild SARS-CoV-2 infections

Ger Rijkers, Jean-Luc Murk, Bas Wintermans, Bieke van Looy, Marcel van den Berge, Jacobien Veenemans, Joep Stohr, Chantal Reusken, Pieter van der Pol, Johan Reimerink

– *medRxiv; https://doi.org/10.1101/2020.06.09.20122036* –

Abstract

We determined and compared the humoral immune response in severe, hospitalized and mild, non-hospitalized COVID-19 patients. Severe patients (n=38) develop a robust antibody response to SARS-CoV-2, including IgG and IgA antibodies. The geometric mean 50% virus neutralization titer is 1:240. SARS-CoV-2 infected hospital personnel (n=24), who developed mild symptoms necessitating leave of absence, self-isolation, but not hospitalization, 75 % develop antibodies, but with low/absent virus neutralization (60% < 1:20). While severe COVID-19 patients develop a strong antibody response, mild SARS-CoV-2 infections induce a modest antibody response. Long term monitoring will show whether these responses predict protection against future infections.

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

Juanjuan Zhao, Quan Yuan, Haiyan Wang, Wei Liu, Xuejiao Liao, Yingying Su, Xin Wang, Jing Yuan, Tingdong Li, Jinxiu Li, Shen Qian, Congming Hong, Fuxiang Wang, Yingxia Liu, Zhaoqin Wang, Qing He, Zhiyong Li, Bin He, Tianying Zhang, Shengxiang Ge, Lei Liu, Jun Zhang, Ningshao Xia, Zheng Zhang

– medRxiv; https://doi.org/10.1101/2020.03.02.20030189 –

Abstract

Background

To investigate the diagnostic value of serological testing and dynamic variance of serum antibody in coronavirus disease 2019 (COVID-19).

Methods

This study retrospectively included 43 patients with a laboratory-confirmed infection and 33 patients with a suspected infection, in whom the disease was eventually excluded. The IgM/IgG titer of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was measured by chemiluminescence immunoassay analysis.

Results

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Conclusions

Viral serological testing is an effective means of diagnosis for SARS-CoV-2 infection. The positive rate and titer variance of IgG are higher than those of IgM in COVID-19.

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