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Comparison of the Elecsys® Anti-SARS-CoV-2 immunoassay with the EDITM enzyme linked immunosorbent assays for the detection of SARS-CoV-2 antibodies in human plasma

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ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
ECLIA
Antibody testing
Serological test

ABSTRACT

Background: Here, we report on a head-to-head comparison of the fully-automated Elecsys® Anti-SARS-CoV-2 immunoassay with the EDITM enzyme linked immunosorbent assays (ELISA) for the detection of SARS-CoV-2 antibodies in human plasma.

Methods: SARS-CoV-2 antibodies were measured with the Elecsys® assay and the EDITM ELISAs (IgM and IgG) in 64 SARS-CoV-2 RT-PCR confirmed COVID-19 patients with serial blood samples (n = 104) collected at different time points from symptom onset. Blood samples from 200 healthy blood donors and 256 intensive care unit (ICU) patients collected before the COVID-19 outbreak were also used.

Results: In COVID-19 patients, the percentage of positive results rose with time from symptom onset, peaking to positivity rates after 15–22 days of 100% for the Elecsys® assay, of 94% for the EDITM IgM-ELISA and of 100% for the EDITM IgG ELISA. In the 104 blood samples, the agreement between positive/negative classifications of the Elecsys® assay and the EDITM ELISAs (IgM or IgG) was 90%. The false positivity rates in the healthy blood donors and the ICU patients were < 1% for the Elecsys® assay and < 3% for the EDITM ELISAs.

Conclusions: Our results indicate a high sensitivity and specificity for the Elecsys® assay and an acceptable agreement with the EDITM ELISAs.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus that causes Coronavirus Disease 2019 (COVID-19), has recently emerged to cause a human pandemic. Besides SARS-CoV-2 RT-PCR testing, currently the method of choice for the confirmation of suspected COVID-19 patients, serological testing is emerging as additional option in COVID-19 diagnostics [1–10].

Recently, Roche Diagnostics (Rotkreuz, Switzerland) has launched the IVD CE-marked Elecsys® Anti-SARS-CoV-2 assay for the qualitative detection of SARS-CoV-2 antibodies on the cobas e immunoassay analyzers. The aim of this study was to compare the clinical performance of the Elecsys® Anti-SARS-CoV-2 assay with the EDITM SARS-CoV-2 IgM and IgG enzyme linked immunosorbent assays (ELISA), which we have recently established in our laboratory.

2. Materials and methods

2.1. Study protocol

This work was performed at the Konventhospital Barmherzige Brueder Linz and Ordensklinikum Linz Barmherzige Schwestern in Linz, Austria. The study protocol was approved by the local ethics committee in accordance with the Declaration of Helsinki.

2.2. Elecsys® Anti-SARS-CoV-2 assay

We measured SARS-CoV-2 antibodies fully-automated on the cobas
EDITM ELISAs (IgM and IgG): negative (OD < positive cutoff); positive (OD ≥ positive cutoff).

Table 1

| Symptom onset | Editm ELISA | Editm ELISA | Editm ELISA | Editm ELISA |
|---------------|-------------|-------------|-------------|-------------|
|               | IgM or IgG  | IgM or IgG  | IgM or IgG  | IgM or IgG  |
| <5 (days)     | n (%)       | n (%)       | n (%)       | n (%)       |
|               | n negative  | n negative  | n negative  | n negative  |
|               | n positive  | n positive  | n positive  | n positive  |
| 34 (100%)     | 33 neg. (97.1%) | 32 neg. (94.1%) | 33 neg. (97.1%) | 31 neg. (91.2%) |
| 1 pos. (2.9%) | 2 pos. (5.9%) | 1 pos. (2.9%) | 3 pos. (8.8%)  |
| 5–10 (days)   | 35 (100%)   | 17 neg. (48.6%) | 22 neg. (62.9%) | 18 neg. (51.4%) |
|               | 18 pos. (51.4%) | 13 pos. (37.1%) | 13 pos. (37.1%) | 17 pos. (48.6%) |
| >10–15 (days) | 17 (100%)   | 4 neg. (23.5%) | 4 neg. (23.5%) | 3 neg. (17.6%) |
|               | 13 pos. (76.5%) | 13 pos. (76.5%) | 14 pos. (82.4%) | 14 pos. (82.4%) |
| >15–22 (days) | 18 (100%)   | 0 neg. (0%)   | 1 neg. (5.6%)  | 0 neg. (0%)   |
|               | 18 pos. (100%) | 17 pos. (94.4%) | 18 pos. (100%) | 18 pos. (100%) |

*Elecsys* assay: negative (COI < 1.0); positive (COI ≥ 1.0).

Table 2

| Symptom onset | Editm ELISA | Editm ELISA | Editm ELISA | Editm ELISA |
|---------------|-------------|-------------|-------------|-------------|
|               | IgM or IgG  | IgM or IgG  | IgM or IgG  | IgM or IgG  |
| <5 (days)     | n (%)       | n (%)       | n (%)       | n (%)       |
|               | n negative  | n negative  | n negative  | n negative  |
|               | n positive  | n positive  | n positive  | n positive  |
| 34 (100%)     | 33 neg. (97.1%) | 32 neg. (94.1%) | 33 neg. (97.1%) | 31 neg. (91.2%) |
| 1 pos. (2.9%) | 2 pos. (5.9%) | 1 pos. (2.9%) | 3 pos. (8.8%) |
| 5–10 (days)   | 35 (100%)   | 17 neg. (48.6%) | 22 neg. (62.9%) | 18 neg. (51.4%) |
|               | 18 pos. (51.4%) | 13 pos. (37.1%) | 13 pos. (37.1%) | 17 pos. (48.6%) |
| >10–15 (days) | 17 (100%)   | 4 neg. (23.5%) | 4 neg. (23.5%) | 3 neg. (17.6%) |
|               | 13 pos. (76.5%) | 13 pos. (76.5%) | 14 pos. (82.4%) | 14 pos. (82.4%) |
| >15–22 (days) | 18 (100%)   | 0 neg. (0%)  | 1 neg. (5.6%)  | 0 neg. (0%)  |
|               | 18 pos. (100%) | 17 pos. (94.4%) | 18 pos. (100%) | 18 pos. (100%) |

*Elecsys* assay: negative (COI < 1.0); positive (COI ≥ 1.0).

Table 3

| Blood donors | n (%)       | n negative (%) | n positive (%) |
|--------------|-------------|----------------|---------------|
| 200 (100%)   | 200 neg. (100%) | 199 neg. (99.5%) | 198 neg. (99%) |
| 0 pos. (0%)  | 1 pos. (0.5%) | 522 neg. (98.4%) | 233 neg. (98.8%) |
| 1 pos. (0.4%)| 4 pos. (1.6%) | 3 pos. (1.2%) | 7 pos. (2.7%) |
| ICU patients | 256 (100%)   | 255 neg. (99.6%) | 253 neg. (98.8%) |
| 1 pos. (0.4%)| 4 pos. (1.6%) | 3 pos. (1.2%) | 7 pos. (2.7%) |

*Elecsys* assay: negative (COI < 1.0); positive (COI ≥ 1.0).

n negative (%) n positive (%) n negative (%) n positive (%) n negative (%) n positive (%) n negative (%) n positive (%) n negative (%) n positive (%)
cohorts of 200 healthy blood donors and 256 intensive care unit (ICU) patients, which were recruited prior to the COVID-19 outbreak (December 3rd 2019). For further details on the clinical study see supplementary data.

3. Results

Table 1 shows low true positivity rates of 3% for the Elecsys® assay and of 9% for the EDITION ELISAs (IgM or IgG) within the first 5 days after symptom onset in the 64 patients with SARS-CoV-2 RT-PCR confirmed COVID-19. In the COVID-19 patients, the percentage of positive results rose with time from symptom onset, peaking to positivity rates after 15–22 days of 100% for the Elecsys® assay, of 94% for the EDITION IgM-ELISA and of 100% for the EDITION IgG ELISA (Table 1). In the 104 blood samples, the overall agreement between positive/negative classifications of the Elecsys® assay and the EDITION ELISAs was 90% for IgM or IgG (Table 2).

The false positivity rates in the healthy blood donors and the ICU patients were < 1% for the Elecsys® assay and < 3% for the EDITION ELISAs (Table 3).

In the supplementary data, we report the quantitative results of the Elecsys® assay and the EDITION ELISAs in the cohort of patients with SARS-CoV-2 RT-PCR confirmed COVID-19, in the healthy blood donors as well as in the intensive care patients (Supplementary Table 1–3).

4. Discussion

The clinical evaluation of the Elecsys® assay revealed very high true positivity rates (i.e. seroconversion rates) of 100% after 15–22 days in the confirmed COVID-19 patients. The false positivity rates of the Anti-SARS-CoV-2 assay were < 1% in the healthy blood donors and in the ICU patients. As stated above in the method section, the Elecsys® assay has been designed at high specificity for detection of mature/late antibodies which are predominantly, but not exclusively, IgG. Overall, we found an acceptable agreement between the Elecsys® assay and the EDITION ELISAs (IgM or IgG) in the confirmed COVID-19 patients.

Of note, with the Elecsys® assay and the EDITION ELISAs, we only report antibody binding to the recombinant nucleocapsid protein (N) and we did not perform neutralization assays in our SARS-CoV-2 RT-PCR confirmed patients. At the limit of detection we found surprisingly low CVs. We assume that these low CV’s are due to the absence of SARS-CoV-2 antibodies in the negative plasma pool. A limitation of our study might be that the plasma aliquots of the healthy blood donors and the ICU patients have been stored for a prolonged time at −80 °C.

The Elecsys® assay and the EDITION ELISAs are currently approved as qualitative assays. However, when looking at the quantitative data in Supplementary Table 1, we found a clear antibody response in SARS-CoV-2 antibody positive COVID-19 patients from < 5 days until > 15–22 days after symptom onset, indicating that these assays might be also suitable for serial measurements. In line with our findings, a very recent work on the antibody responses to SARS-CoV-2 in patients with COVID-19 demonstrated a similar approach using measured chemiluminescence values divided by the cutoff for reporting of SARS-CoV-2 antibody quantitative values/titer [8]. They further showed that serial serological testing may be helpful for the diagnosis of suspected COVID-19 patients with negative SARS-CoV-2 RT-PCR results and for the identification of asymptomatic infections in close contacts [8].

In conclusion, our results indicate a high sensitivity and specificity for the Elecsys® assay and an acceptable agreement with the EDITION ELISAs.

Research funding: Roche Diagnostics provided reagents for the Elecsys® Anti-SARS-CoV-2 measurements free of charge. The company did not play a role in (1) the design of the study; (2) data collection, analysis and interpretation.

Employment or leadership: None declared.

Honoraria: Benjamin Dieplinger and Thomas Mueller have received speaking fees from Roche Diagnostics.

CRediT authorship contribution statement

Margot Egger: Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. Christian Bundschuh: Methodology, Formal analysis, Writing - original draft, Writing - review & editing. Kurt Wiesinger: Formal analysis, Writing - original draft, Writing - review & editing. Christian Gabriel: Formal analysis, Writing - review & editing. Martin Clodi: Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing. Thomas Mueller: Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing. Benjamin Dieplinger: Conceptualization, Methodology, Resources, Formal analysis, Validation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2020.05.049.

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