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Short communication

The Coris BioConcept COVID 19 Ag Respi-Strip, a field experience feedback

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ABSTRACT

This communication described how the Coris BioConcept COVID-19 Ag Respi-Strip test (Coris-Ag) was implemented in the workflow of our clinical microbiology laboratory for COVID-19 diagnosis. The diagnostic performance statistics (sensitivity, specificity) of the Coris-Ag were evaluated against a gold standard, the RealStar SARS-CoV-2 RT-PCR kit 1.0. Additionally, the effect of reading the Coris-Ag results at 30 min was compared to reading at 15 min. The Coris-Ag was performed on a total of 294 patients during two periods; 158 patients were tested during period 1 at the peak of the pandemic (April 6th to April 10th 2020) which returned a positivity rate of 17.1 %, and 136 patients during period 2 (April 12th to April 16th 2020) which returned a positivity rate of 11 %. Compared to the RT-PCR, the 15-minute Coris-Ag readings resulted in a sensitivity of 59.3 % with a 100 % specificity for the period 1 patients (n = 158) while the sensitivity decreased to 20 % for the period 2 patients (n = 136). The overall sensitivity was 38.1 % for both periods (n = 294). The corresponding 30-minute readings produced a 7 % increase in sensitivity with a specificity of 100 % (n = 294). The sensitivity of the strip test (15-min reading) for high viral loads (Ct <25) was 84.6 %.

The severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) pandemic is still on-going with a worldwide infection rate of 188,367,022 cases and 4,058,263 deaths (John Hopkins Coronavirus Resource Center, 2021).The Coris BioConcept COVID-19 Ag Respi-Strip test (Coris-Ag) is an immuno-chromatographic test that is easy to use and fast (<1 min of handling time per test followed by a 15-min incubation). For comparison, the RT-PCR assay has a time-to-result of two hours (van Kasteren et al., 2020). The Coris-Ag kit can be stored at room temperature and can be performed on the same clinical samples to be used for the RT-PCR test. According to the manufacturer's product notes (COVID-19 Ag Respi-Strip - COVID-19 Antigen rapid test, 2021), the detection limit of Coris-Ag was determined to be 5×10^3 plaque-forming units/mL using a SARS-CoV-2 virus standard. In this context, the usefulness of the Coris-Ag was evaluated during the first peak of the COVID-19 pandemic in France (6th April 2020 to 10th April 2020).

The Coris-Ag was subjected to an initial diagnostic performance evaluation before being implemented under real-life conditions at the clinical microbiology laboratory of Groupe Hospitalier Paris Saint-Joseph, Paris, France. The initial evaluation and the real-life implementation were performed in the exact same manners except that during the initial evaluation, the results were not given to the physician. All samples tested were naso-pharyngeal swabs in Universal Transport Medium (UTM-RT, Copan, USA) from patients with clinical suspicion of COVID-19 from the Groupe Hospitalier Paris Saint-Joseph. The diagnostic performance statistics of Coris-Ag were obtained using the RealStar SARS-CoV-2 RT-PCR kit 1.0 (Altona Diagnostics GmbH, Hamburg, Germany) RT-PCR assay as the gold standard. The initial evaluation was conducted on 52 nasopharyngeal samples collected from patients and based on the 15-min reading of the Coris-Ag. When the samples arrived in the laboratory, the Coris-Ag was performed and then RT-PCR analysis

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was performed using the same sample. No changes to the supplier's data were made for the Coris-Ag or for the RT-PCR analysis.This same workflow was used for the real-life conditions testing. The evaluation under real-life conditions was conducted on a total of 294 different patients over two periods of 1 week each. Period 1 (April 6th to April 10th 2020) was at the peak of the pandemic and 158 patients were tested. Period 2 was the following week (April 12th to April 16th 2020) with 136 patients tested.

The Coris-Ag was prospectively evaluated based on reading the test results at 15 min as recommended by the manufacturer, as well as on a second reading at 30 min. The results of the RT-PCR assays were based on cycle threshold (Ct) values, with Ct >37 as being virus-negatives as specified by the French Society of Microbiology ("Avis du 25 septembre 2020 de la Société Française de Microbiologie (SFM) relatif à l'interprétation de la valeur de Ct (estimation de la charge virale) obtenue en cas de RT-PCR SARS-CoV-2 positive sur les prélèvements cliniques réalisés à des fins diagnostiques ou de dépistage,", 2021). The diagnostic performance statistics of Coris-Ag were then calculated for the 15-min and 30-min readings, and for the Periods 1 and 2 patients separately. The RT-PCR virus-positive samples from the real-life screening were classified semi-quantitatively according to the ranges of cycle threshold (Ct) values as follow:

- Very high viral load (< 25 Ct)
- High viral load (25 < Ct < 30)
- Medium viral load (30 < Ct < 35)
- Low viral load (Ct >35)
- Negative viral load (Ct >37)

The diagnostic performance of Coris-Ag was also evaluated based on only those RT-PCR assays with a PCR Ct < 25 as being real positives.

The initial evaluation of the Coris-Ag system based on the 15-min reading on the 52 samples produced eight true positives, 0 false positive, 41 true negative and three false negatives (Table 1, Column 2). The resultant sensitivity was 72 %, specificity was 100 %, positive predictive value (PPV) was 100 % and negative predictive value (NPV) was 93 %. The diagnostic performance statistics of the Coris-Ag system obtained from the real-life screening of the 294 patients were calculated for the 15-min and 30-min readings, and the Periods 1 and 2 screenings (Table 1, Columns 3, 4, 5 and 6, respectively). The results based on the 15-min readings showed that 16 samples were diagnosed as positive (positivity rate = 5.4 %). The sensitivity was 38.1 % and the specificity was 100 %. The number of false negatives was 26. The second readings at 30 min produced 19 positive samples (positivity rate = 6.5 %), all of which were confirmed to be positive by the RT-PCR assay which produced a positivity rate of 14.3 % (42/294) over the two-week study period. Thus, the specificity of the 30-min readings remained at 100 % and the sensitivity was increased to 45.2 %. An analysis of the diagnostic statistics from Periods 1 and 2 (Table 1, Columns 5 and 6, respectively) showed that the RT-PCR assay produced a positivity rate of 17.1 % for Period 1 and 11 % for Period 2. The corresponding positivity rates of Coris-Ag were 10.1 % for Period 1 and 2.2 % for Period 2, and the sensitivity was 59.3 % for Period 1 and 20 % for Period 2.

When the 42 RT-PCR-positive samples from the two-week real-life screening were classified semi-quantitatively according to the ranges of cycle threshold (Ct) values and correlated to the corresponding Coris-Ag assay results, 11 of the 19 Coris-Ag-positive samples (30-min readings) were of very high virus loads (Ct <25) while the remaining eight were of high virus loads (Ct between 25 and 29) (Table 2). Of the 26 false negative samples (Coris-Ag-negative but PCR-positive), 2 were indicative of very high virus loads, 9 of high virus loads, eight of medium virus load and 7 indicating low virus load (Table 2). The data in Table 2 indicated that if the samples were of very high viral loads (Ct < 25), the sensitivity of Coris-Ag was 84.6 %, while for samples of medium or low virus loads, the sensitivity could be 0% (Table 2). Finally, the three extra Coris-Ag positives observed at 30-min reading (negative at 15-min reading) were all of high virus loads (Ct between 25 and 29).

The results of the initial evaluation were consistent with those of the evaluations conducted in two teaching hospitals in Belgium (Brussels and Liege) on 99 and 132 patients, respectively (COVID-19 Ag Respi-Strip - COVID-19 Antigen rapid test, 2021). Their results showed a specificity of 100 % and sensitivities of 60 % and 60.3 %, respectively.

Table 1
Diagnostic performance statistics of the Coris BioConcept COVID-19 Ag Respi-Strip test compared to the RealStar SARS-CoV-2 RT-PCR kit 1.0 assay obtained from the initial evaluation of 52 samples and the two-week real-life screening of 294 samples.

Coris-Ag diagnostic performance statistics[a]	Initial evaluation (15-min reading) (n = 52)	Coris-Ag: 15-min reading[b] (n = 294)	Coris-Ag: 30-min reading[b] (n = 294)	Period 1[c] (n = 158)	Period 2[c] (n = 136)
True positive	8	16	19	16	3
True negative	41	252	252	131	121
False positive	0	0	0	0	0
False negative	3	26	23	11	12
Sensitivity (%)	72.0	38.1	45.2	59.3	20.0
Specificity (%)	100	100	100	100	100
PPV (%)	100	100	100	100	100
NPV (%)	93.0	90.6	91.6	92.2	91.0
Positivity rate of RT-PCR (%)[d]	22.6	14.3	14.3	17.1	11.0
Positivity rate of Coris-Ag[d] (%)	15.4	5.4	6.5	10.1	2.2
Coris-Ag accuracy[e] (%)	94.2	91.2	92.2	93.0	91.2

PPV = positive predictive value and NPV = negative predictive value.
Accuracy = (true positive + true negative/true positive + false negative + true negative + false positive).
[a] Performance statistics of Coris-Ag were calculated for both 15- and 30-min readings and for Periods 1 and 2.
[b] The 15-min and 30-min reading data were of all the 294 patients over the two weekly periods.
[c] Periods 1 and 2 data were based on the 30-min readings.
[d] Positivity rates indicated for RT-PCR and Coris Ag were for the period of the initial evaluation (column 2), either the whole two weeks (columns 3 and 4) or for each Periods 1 and 2 separately (columns 5 and 6).
[e] Accuracy: overall probability that a patient will be correctly classified.

Table 2
Relationship between indicative virus load (Ct values) of the PCR-positive samples and the resultant diagnostic performance of Coris-Ag [a].

Viral load category of PCR-positive samples	Total PCR (true) positive[b]	Positive Coris-Ag (% of Ct category)[c]	Negative Coris-Ag (% of false negatives)[d]
Very high viral load (Ct<25)	13	11 (84.6)	2 (8.7)
High viral load (25 < Ct<30)	14	8 (57.1)	6 (26.1)
Medium viral load (30 < Ct<35)	8	0 (0)	8 (34.8)
Low viral load (Ct > 35)	7	0 (0)	7 (30.4)
Total	42	19 (45.2)	23 (100)

[a] Based on the 30-min readings of the 294 samples.
[b] Positives identified by the gold standard RT-PCR assay.
[c] Percentages were of the total number of positives in each virus load category by the gold standard RT-PCR assay.
[d] Total number of false-negatives was 23.

The implementation of Coris-Ag went smoothly in the clinical microbiology laboratory. Since the PPVs of Coris-Ag were 100 % (*i.e.*, no false positives) in all the test groups in this study (Table 1), each Coris-Ag-positive result did not require RT-PCR confirmation and was reported in the patient's medical record and communicated to the referring physician. This would allow a rapid transfer of the patient to dedicated COVID wards. In the case of a negative result, the result was not communicated to the physician nor recorded in the medical chart. In that case, a final diagnosis should be made according to the RT-PCR result.

The Coris-Ag detected only 38 % (16/42) of the true positive samples, or 6% (16/294) of the patients, by the 15-min reading recommended by the manufacturer. These were mainly those with the highest viral loads. For these patients, diagnostic results were available rapidly, facilitating their early referral to the right COVID area. It should be stressed that the high sensitivity of Coris-Ag, obtained when the PCR Ct <25, is of high healthcare value since it allows a quick but reliable diagnosis of patients with very high viral loads. Indeed, COVID-19 patients with severe disease symptoms had significantly higher viral loads than those with mild disease in respiratory samples and therefore, could be diagnosed reliably and quickly using Coris-Ag instead of RT-PCR (Zheng et al., 2020). However, this study showed that the Coris-Ag test sensitivity obtained during Period 2 was unacceptably low (20 %) when COVID-19 prevalence was low (11 %), suggesting its limitation as a screening program outside of the pandemic peak. This phenomenon may be explained by the observation that a decrease in the number of patients with high viral loads was associated with a decrease of overall disease incidence (data not shown). Scohy et al. (2020) found a low diagnostic sensitivity of 30.2 % in their Coris-Ag screening of 148 samples, and Blairon et al. (2020) reported a median sensitivity of 23.9 % for Coris-Ag test, both of which are consistent with the findings of this study. Similarly, Lambert-Niclot et al. (2020) obtained a sensitivity of 50 % (47 Coris-Ag-positives on 94 PCR-positives samples) and found a corresponding increase in sensitivity with very high viral loads (Ct <25). The results of this study confirmed this trend on a larger cohort.

This study is the first that evaluated a 30-min reading time in addition to a 15-min reading time, resulting in a 7% increase (38.1%–45.2%) in sensitivity. These results indicated that extending the reading time from 15 min to 30 min could increase the sensitivity. This is encouraging but need to be confirmed by a larger cohort in order to avoid false positive.

Based on the results of this study, the Coris-Ag system should be used in some developing countries where RT-PCR may not be easily or extensively available. Another potential for this test is for it to be used directly by physicians as a doctor's test, mostly in geriatrics long-time care in case of local clusters developing. The cost range of Coris-Ag is between 5–10 USD per test, depending on the volume ordered. This is about four to five times cheaper than a RT-PCR assay. The extra cost of the PCR assay must be taken into account and could be reduced if Coris-Ag is used for the diagnosis of patients within the first few days of the onset of clinical symptoms, for patients with severe disease and during periods when the prevalence of COVID is high. Negative results from these preliminary screening protocols should then be retested by RT-PCR as proposed by Mertens et al. (Mertens et al., 2020). Thus, despite its limitations, the Coris-Ag system could find a use in laboratories not equipped with RT-PCR or as a point-of-care doctor's test on the condition that negative results be confirmed by RT-PCR.

Declaration of Competing Interest

The authors report no declarations of interest.

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