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Diagnostic Strategies of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: Operational Recommendations for Health Professionals

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Due to the massive impact of the coronavirus disease 2019 (COVID-19) pandemic worldwide, the

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accurate and early diagnosis and isolation of infected individuals remains the main way of rapidly curtailing the extension of the disease. The increasing incidence of mutations in the virus RNA sequence represents the principal challenge for the use of molecular approaches for COVID-19 diagnosis. Additionally, because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreads differently to that of its *Coronaviridae* counterparts, unconventional strategies and diagnostic algorithms must be utilized and comprehensively expanded. Therefore, in this study, we sought to conduct a detailed in-depth investigation using many scientific interfaces to i) determine the fastest, most cost-effective, and most comprehensive diagnostic techniques, and ii) identify the proper specimens used for SARS-CoV-2 detection. To accomplish that, we reviewed previous studies investigated for the diagnosis of COVID-19. These strategies are organized to help health professionals and policymakers to quickly choose and apply the appropriate diagnostic approaches.

Keywords: Diagnosis; SARS-CoV-2; molecular tests; serological tests; pneumonia.

1. INTRODUCTION

The number of emerging viral diseases has escalated in the last two decades, and these diseases have become a serious public health concern worldwide. This is particularly true of infections associated with human coronaviruses (HCoVs), including severe acute respiratory syndrome coronavirus (SARS-CoV or recently renamed as SARS-CoV1), which erupted in China in 2002 [1], and Middle East respiratory syndrome coronavirus (MERS-CoV), initially isolated in Saudi Arabia in 2012 [1,2]. Recently, a new coronavirus strain has been reported, and has rapidly spread worldwide since it first emerged in China. The COVID-19 is caused by the emerging virus SARS-CoV-2. On December 31, 2019, the World Health Organization (WHO) was alerted to reports of many cases of unexplained pneumonia in the city of Wuhan (Hubei Province of China). To date, a total of 219 countries and territories had been affected. Globally, around 104 million individuals have been infected, resulting in approximately 2.28 million deaths [3] During the spring of 2020, Europe became the focus of infection; thereafter, since the summer of 2020, the USA, India and Brazil had become the most affected countries [3].

Symptoms of COVID-19 caused by the new strain are not unique, but are similar to those resulting from various bacterial and viral infections attacking the respiratory tract [4]. Remarkably, the SARS-CoV-2 infection is likely an airborne disease and has been first described to occur through close contact with both symptomatic and asymptomatic carriers [5,6] To date, a gold-standard diagnostic approach identifying infected people is still elusive. However, using viral genome for Reverse transcription-polymerase chain reaction (RT-PCR) remains the most commonly used approach for the identification of infected persons [7]. The RT-PCR test can be performed on different respiratory specimens, such as nasopharyngeal swabs and sputum. The results are usually available within hours to 2 days [8].

On the other hand, serological approaches include various methods by which several viral infections are being diagnosed. Serological tests aim to identify the presence of antibodies, microbial markers, and sometimes, as in the case of autoimmune diseases, autoantibodies. Several countries are competing in developing and improving the sensitivity of rapid serological tests for use on a large scale. For example, the American Food and Drug Administration approved the first rapid serological antibody test for the diagnosis of COVID-19 infection in mid-March of 2020, while the first antigen test was approved on May 9, 2020 [9,10].

The prevention of SARS-CoV-2 transmission is crucial for the elimination and control of the COVID-19 infection. However, identifying rapid, simple, and highly sensitive diagnostic procedures and algorithms to enable the isolation of infected individuals, thereby preventing further viral transmission, remains a major challenge. False-negative results may occur, and not quarantining infected people would constitute a major setback for the curtailment of viral transmission [11,12]. Noteworthy, the large global need for testing materials due to the COVID-19 pandemic has resulted in a lack of molecular diagnostic reagents. In addition, diagnostic equipment is still expensive and not available for most laboratories. Consequently, there is an urgent demand for a sensitive, fast, and economical method that does not need a lot

of reagents. Additionally, Researchers usually use respiratory specimens to assess the assays used for the diagnosis of SARS-CoV-2. However, non-respiratory specimens such as plasma, urine, feces, and rectal swabs can also be evaluated for the detection of the virus. Our review aimed to provide an in-depth assessment of the currently available diagnostics strategies used by health authorities according to clear indicators (sensitivity, specificity, turnaround time, target specimens, and target genetic region or antigens/antibodies). This could help save time for healthcare providers, accelerate patient treatment, limit the progression of the virus, and decrease the human and economic impact of this crisis. Nevertheless, owing to the current containment measures, a precise and fast *in vitro* testing system for a detailed analysis of COVID-19 remains elusive, and broad electronic research, using a range of scientific interfaces, is necessary to answer debated questions.

1.1 Molecular Tests

The most widely used method for diagnosing viral infections is amplification of viral genomic sequences using RT-PCR techniques. These techniques are known to be sensitive and specific to each type of virus. They are also quantitative and allow the monitoring of antiviral treatment effectiveness. However, the molecular methods currently being used for the diagnosis of COVID-19 infection are more likely not appropriate enough to detect small amounts of viral genomic materials present in a given specimen [13]. On January 23, 2020, a multinational group of scientists published a standardized protocol for SARS-CoV-2 detection employing Real-Time PCR assays targeting the SARS-CoV-2 *E*, *N* and *RdRp* genomic sequences [14]. Since then, several additional PCR and molecular techniques have been developed to improve the sensitivity and specificity of SARS-CoV-2 detection and reduce the associated costs and reaction times. In this review, we screened and assessed RT-PCR, LAMP, and multiplex RT-PCR assays, as summarized in Table 1 [15–22].

Chan and colleagues assessed an RT-PCR procedure that used RNA extracts from *in vitro* culture lysates and targeted the RNA-dependent RNA polymerase/helicase (*RdRp/Hel*), *S*, and *N* genes [15], and compared the findings with those previously reported for *RdRp* gene RT-PCR (14). The results determined that *RdRp/Hel* gene-targeting RT-PCR had the lowest limit of detection (LOD) of 1.8 TCID50/mL (tissue culture infection dose 50% per mL) [15]. Furthermore, the authors assessed 120 respiratory and 153 non-respiratory specimens collected from 15 different laboratories for confirmed COVID-19 patients using *RdRp/Hel* RT-PCR. The authors reported that the positivity rates using this assay were 85% and 11.1% in comparison to the 60.8% and 2.6% of the *RdRp* RT-PCR assay for the respiratory and non-respiratory specimens, respectively. To evaluate the specificity of the assay, they tested 17 human viruses using the designed SARS-CoV-2 primer sets. The authors confirmed that *RdRp/Hel*-, *S*-, and *N*-specific gene primers can be specifically used for the diagnosis of SARS-CoV-2 as no PCR product could be observed for other corona viruses, whereas cross-amplification was only noted using primers specific for *RdRp* [15]. Similarly, Yip et al. generated a highly robust RT-PCR assay targeting the nonstructural gene 2 (*nsp2*) with a sensitivity and a specificity of 100% and in comparison with the assay targeting the *RdRp/Hel* as shown in Table 1 [23]. Additionally, the developed *nsp2* gene-targeting assay is specific for the SARS-COV2 *nsp2* gene as compared with 17 other human viruses, including corona viruses [23]. Another study in the USA conducted a comparative analysis among the primer/probe sets for the *RdRp* and *E* genes recommended by the Corman team; the primer/probe sets for the *N1*, *N2,* and *N3* genes recommended by the CDC; and those from the commercial BGI RT-PCR SARS-CoV-2 detection kit [20]. Nasopharyngeal and/or oropharyngeal swabs obtained from10 confirmed infected people and 22 negative samples were used in this investigation. RT-PCR targeting the *E* gene recommended by the Corman team and the *N2* gene recommended by the CDC showed a LOD of 6.3 copies/reaction with 100% sensitivity and specificity (Table 1). The authors emphasized the high efficacy of RT-PCR for direct diagnosis of COVID-19, especially in the early stages of infection [20].

Despite its robustness and the ability to amplify target nucleic acids to a similar magnitude, with a reasonable LOD, traditional RT-PCR methods still require complicated equipment due to poor specificity of target sequence selection, highly qualified personnel, and it is relatively time-consuming (about 1.5–2 h) [24,25]. Moreover, the total turnaround time for RT-PCR results (1 to 2 days) can still be a disadvantage, especially when the spread of the virus continues to show large daily increases [3]. Consequently,

researchers have strived to develop faster molecular strategies for diagnosing COVID-19, such as the loop-mediated isothermal amplification (LAMP). This approach, which uses isothermal conditions and 4-6 specifically designed primers, can speedily amplify a distinct DNA region with high specificity [26]. LAMP could be coupled with reverse transcription (RT-LAMP) to allow RNA detection [27]. This one-step visual reaction has allowed the diagnosis of COVID-19 within turnaround time of 26-45 minutes [16,18,19,22,28]. Two studies using RT-LAMP targeting the SARS-CoV-2 *N* gene reported a LOD of approximately 100 copies per reaction after 30 to 40 minutes, allied with colorimetric visualization [19,21]. These two assays for COVID-19 diagnosis have high specificity for SARS-CoV-2 when tested against different human respiratory viruses including SARS-CoV [19,21]. Another locus in the genome, the coding region of the open reading frame 1ab (ORF1ab), has also been evaluated for the detection of SARS-CoV-2 using RT-LAMP [18]. The result of this assay can be delivered within 30 to 45 minutes with a LOD of 304 copies/ reaction. Notably, the assay can be performed on different samples such as serum, urine, saliva, and oropharyngeal and nasopharyngeal swabs [18]. In this context, using RT-LAMP and targeting the same ORF1ab region, Yan et al. reported a LOD of 20 copies/reaction. Interestingly, this group also reported that the LOD for when the *S* gene was targeted was 10 folds higher [2]. The authors used bronchoalveolar swabs and lavage fluid specimens collected from 130 patients presumed to be SARS-COV-2-positive. For trial assessment, they compared the RT-PCR and RT-LAMP results, with both methods yielding 58 positive and 72 negative patients. Nevertheless, the RT-LAMP test developed by Yan and his colleagues targeting ORF1ab region and *S* gene could detect SARS-COV-2 in only 26 minutes with a sensitivity and specificity of 100% [22]. Interestingly, a cooperative Chinese–UK study proposed four sets of RT-LAMP composed of a mix of six primers targeting the SARS-CoV-2 ORF1ab, *S*, and *N* gene loci [16]. Hence, it is possible to amplify RNA directly from the sample using a one-step reaction without RNA extraction [16]. This study reported a LOD of approximately 2 copies/reaction, a turnaround reaction time of approximately 30 minutes, and the obtained results were consistent with traditional RT-qPCR. Collectively, these studies indicate that RT-LAMP can be an accurate alternative molecular tool for the diagnosis of SARS-COV-2 with low cost and greatly improve the turnaround time [16,18,19,22,28].

In the same context, multiplex PCR allows the simultaneous amplification of several distinct DNA fragments in a single reaction tube, using pairs of primers specific for different loci. The amplification conditions are fixed for the same tube in which several different reactions take place, and the choice of conditions results from thorough testing [29]. In particular, the choice of primer pairs must be rigorous to find a balance between the annealing temperature and the optimum elongation time for each PCR reaction. Ishige et al. developed a multiplex RT-PCR-based method as a quick, sensitive, and specific diagnosis tool of SARS-COV-2. The authors targeted three genes, namely the *Sarbecovirus*-specific *E* gene, the SARS-COV-2-specific *N* gene, and the human *ABL1* gene, which was used as internal control. For the evaluation of the multiplex PCR, the authors tested 4 SARS-COV-2-positive and 20 negative specimens that had been confirmed by standard RT-PCR, and obtained a compatible result between the simplex RT-PCR and the multiplex RT-PCR, with the latter showing a LOD of 25 copies/reaction (Table 1) [17]. Nevertheless, the number of samples investigated in this study was very low and a rigorous evaluation of the RT-PCR multiplex methodology is required to validate these results.

Molecular tests may be of greatest help at the onset of infection. They can confirm the presence of the virus up to 2 days before the beginning of symptoms, unlike serological tests where the antibodies will not be measurable for at least 6 days after the symptoms first appear [30]. In contrast, the SARS-CoV-2 viral load has been reported to be undetectable using molecular tools 21 to 35 days after symptom onset. Consequently, molecular tests cannot detect previous infections [30], and other diagnostic tests are required for this purpose. Among the molecular techniques evaluated to date, RT-LAMP may bring the most benefits due to its simplicity, robustness, and low cost. It has the capacity to be used as a simple screening test in the field or at the clinician's care point. Because of the isothermal conditions used for RT-LAMP, this approach is also cost-effective as it does not require expensive thermal cyclers. Importantly, LAMP was one of the molecular methods recommended by the WHO for the detection and identification of *Plasmodium* [31]. In view of these listed advantages, we recommend the use

of this molecular technique for the mass screening of COVID-19.

1.2 Serological Tests

Serology is a commonly used biological method for establishing diagnoses. It consists of the analysis of serum to detect specific antibodies or circulating antigens that may be linked to the presence of specific pathogens (mainly bacteria and viruses, but sometimes also parasites). Table 2 summarizes the four different serological tests investigated during the first year of the COVID-19 pandemic, namely, (1) the chemiluminescence immunoassay (CLIA), (2) enzyme-linked immunosorbent assay (ELISA), (3) rapid antigen test, (4) and lateral flow immunoassay (LFIA), which have been tested for the diagnosis of COVID-19 [32–37]. During viral infections, antibodies are not detectable until at least 6 to 10 days after the onset of the first symptoms; immunoglobulin M (IgM) and A (IgA) are the first to appear, followed by immunoglobulin G (IgG). Liu et al. performed a time-course assessment of the serum levels of IgM and IgG for 212 COVID-19 verified cases using ELISA and recombinant S and N proteins. In this study, the positivity rate of the IgM–IgG combination was approximately 60% from day 0 to day 10 and 90% from day 16 to day 20 from the onset of the first symptom, respectively. Starting from day 35, the positivity rate was 100% and 71% for IgG and IgM, respectively. Moreover, ELISA sensitivity using the recombinant S protein was considerably higher than that using the recombinant N protein (Table2) [33]. Similarly, a retrospective study by Jin et al. using CLIA confirmed that the titer variance and positivity rate of IgM were lower than those of IgG in COVID-19 subjects (Table2) [32]. A serological test could also be applied in large-scale seroepidemiological studies [34,36]. Perera et al. developed an efficient IgG ELISA-based seroepidemiological test using the RNA-binding domain (RBD) of the spike protein as a recombinant antigen to screen sera for SARS-CoV-2-specific antibodies [38]. The developed ELISA was accurately positive with no noticeable cross-reactivity after a month of illness commencement. To confirm the obtained results, the authors used a 90% plaque reduction neutralization test (PRNT90) and microneutralization tests. These two reference techniques are used for the detection and measurement of antibodies that can neutralize pathologic viruses [36]. Another serological test, the LFIA using lanthanide-doped polystyrene nanoparticles, has been applied to detect anti-SARS-CoV-2 IgG in human serum [34] (Table2). The main advantage of this assay is its speed, allowing results to be delivered within just10 minutes. However, the assay was tested on a very small number of samples (only seven positive SARS-CoV-2 samples previously verified by RT-PCR) and therefore no conclusions can be drawn due to its weak reliability and accuracy [34]. A larger number of samples must be tested using LFIA to correctly assess the robustness of this technique. It is worth mentioning that the antibody tests should not be considered for the diagnosis of COVID-19 patients, but only to monitor the progression of COVID-19 and to assess the patient's response to the given therapy [10,33].

Immunoassays detecting antibodies to viruses lead to the identification of people evolving an adaptive immune response to both active and previous viral infections [10]. Scientists developed a rapid method for diagnosing SARS-CoV-2 antigen in addition to antibody detection methods. One of the major advantages of the antigen tests is its speed given that the result can be provided within only a few minutes. In April 2020, a Korean team created a promising field-effect transistor (FET)-based biosensing device for detecting SARS-CoV-2 (Table2) [35]. The sensor was fabricated by covering graphene sheets in a FET with an antibody specific for the spike protein of SARS-CoV-2. This responsive immunological diagnostic technique has the ability to detect the spike protein at concentrations of 1 fg/mL in phosphate-buffered saline and 100 fg/mL in transport media. It also displayed LODs of 1.6 plaque-forming units (pfu)/mL in culture medium and 242 copies/mL in clinical samples. Furthermore, the FET technique does not require sample pretreatment or labeling [35]. Antigen tests are essential in the battle against the pandemic caused by the new coronavirus, SARS-CoV-2, owing to their simple design and low production costs when compared with molecular methods. Moreover, they allow the easy identification of infections in real-time [10]. However, an evaluation of the performance of a rapid immunochromatographic test for the detection of SARS-CoV-2antigen relative to RT-PCR yielded a limited sensitivity (30.2%) but high specificity (100%), see Table 2 [37]. Although antigen tests are highly accurate for the detection of SARS-CoV-2, they do not detect all active infections, and their sensitivity is limited when compared against molecular methods. Moreover, even though positive results based on antige

Table 1. Outline of molecular tests for the detection of SARS-COV-2

Technique/ (Country)	Size of tested samples: Control group	Specimen	Specificity/ Sensitivity	Locus	Limit of detection (LOD)/Cross-reactivity	Reaction turnaround time	(Reference)
RT-PCR (China)	23:36	Respiratory tract specimens	Specificity 100% Sensitivity 100%	*Nsp2* gene	1.8 TCID50/mL No cross-reactivity with 17 human viruses	N.D.	[23]
RT-LAMP (UK and China)	8:8	Throat swabs	High specificity High sensitivity	*N* gene (N1 and N15 regions) *S* gene (S17 region) Regions of ORF1ab Human beta-actin primers	80 copies of viral RNA per mL in a sample Or 2 copies in a 25-µL reaction volume /N.D.	20-30 minutes	[16]
Multiplex rRT-PCR (Japan)	30: N.D.	Sputum	High specificity Sensitivity 100%	*Sarbecovirus*-specific *E* gene SARS-CoV-2 specific *N* gene Human *ABL1* gene	21 copies/reaction /N.D.	N.D.	[17]
RT-LAMP (China)	36:20	Throat swabs	High Specificity Sensitivity 100%	*N* gene	118.6 copies/per 25-µL reaction volume /No cross-reactivity with 17 respiratory viruses but not tested with SARS-CoV and MERS-CoV	30 to 40 minutes	[19]
RT-LAMP (Korea)	N.D.	SARS-CoV-2 RNA were isolated from	N.D. N.D.	*N* gene Two regions from *Nsp3*	100 copies per reaction /No cross-reactivity	30 minutes	[21]

Technique/ (Country)	Size of tested samples: Control group	Specimen	Specificity/ Sensitivity	Locus	Limit of detection (LOD)/Cross-reactivity	Reaction turnaround time	(Reference)
		culture media of infected cells.		Two regions from *S gene* One region from *Orf8*	to three other human coronaviruses		
RT-LAMP (China)	58:72	Swabs and bronchoalveolar lavage fluid	Sensitivity 100% (95% CI: 92.3%–100%) Specificity 100% (95% CI: 93.7%–100%)	ORF1ab region *S* gene	ORF1ab-4 20 copies/reaction S-123 200 copies/reaction /No cross-reactivity with 60 human respiratory pathogens	26.28 to 31.16 minutes	[22]
RT-LAMP (Korea)	55:99	Nasal swab	Sensitivity 100% Specificity 98.70%	*N* gene	1×10^3copies per reaction	30 minutes	[28]
RT-PCR (China)	Total 273: N.D. 120 respiratory specimens	Respiratory specimens (Nasopharyngeal aspirate/swab, throat swab, and/or sputum specimens)	Sensitivity 85% Specificity 100%	RdRp/Hel	LOD 1.8 TCID50/mL LOD using in vitro viral RNA transcripts. 11.2 RNA copies/reaction (95% confidence interval, 7.2 to 52.6 RNA copies/reaction). /No cross activity with other respiratory viruses	N.D.	[15]
	153 non-respiratory specimens	Non-respiratory tract specimens	Sensitivity 11% Specificity				

Technique/ (Country)	Size of tested samples: Control group	Specimen	Specificity/ Sensitivity	Locus	Limit of detection (LOD)/Cross-reactivity	Reaction turnaround time	(Reference)
		(urine sample, rectal swab, and feces)	100%	Gene S	LOD 1.8 TCID50/mL LOD using in vitro viral RNA transcripts N.D. /Cross activity		
				Gene N	N.D. LOD 1.8 TCID50/mL LOD using in vitro viral RNA transcripts 21.3 RNA copies/reaction (95% confidence interval, 11.6 to 177.0 copies/reaction) /No cross activity with other respiratory viruses		
RT-PCR (USA)	10:22	Nasopharyngeal or oropharyngeal swabs	Sensitivities 100% at 63 viral copies per reaction Specificities	Corman *E* gene Corman *RdRp* gene CDC *N1* gene CDC *N2* gene BGI kit	6.3 copies/reaction 63 copies/reaction 31.5 copies/reaction 6.3 copies/reaction 12.6	N.D.	[20]

Technique/ (Country)	Size of tested samples: Control group	Specimen	Specificity/ Sensitivity	Locus	Limit of detection (LOD)/Cross-reactivity	Reaction turnaround time	(Reference)
			100%		copies/reaction /No cross activity with other respiratory viruses		
RT-LAMP (USA)	30:30	Serum, urine, saliva, oropharyngeal swabs, and nasopharyngeal swabs	N.D./N.D.	*Nsp3* gene ORF1Ab	304 copies/reaction /No cross-reactivity with MERS-CoV, betacoronavirus England1, or murine hepatitis virus	30 to 45 minutes	[18]

N.D.: not described; RT-LAMP: reverse transcription–loop-mediated isothermal amplification; SARS-CoV: severe acute respiratory syndrome coronavirus; MERS-CoV: Middle East respiratory syndrome coronavirus; RdRp: RNA-dependent RNA polymerase; RdRp/Hel: RNA-dependent RNA polymerase/Helicase; ORF1ab: open reading frame coding region; N: gene encoding the nucleocapsid protein;Nsp2: nonstructural gene 2; Nsp3: nonstructural gene 3; S: gene encoding the spike protein; E: envelope protein gene; CDC: Centers for Disease Control and Prevention; LOD: limit of detection; TDCI 50%: 50% tissue culture infective doses.

Table 2. Outline of rapid serological tests for the detection of SARS-COV-2

Method/ (Country)	Size of tested samples: Control group	Specimen	Antigen or antibody types	Sensitivity/Specificity	Reference
Chemiluminescence immunoassay (CLIA) (China)	43: 33	Serum	Nucleocapsid protein Spike protein	48.1% IgM antibodies sensitivity 100% IgM antibodies specificity 50% IgM antibodies positive rate before and after conversion to SARS-cov2-virus-negative. 88.9% IgG antibodies sensitivity	[32]

Method/ (Country)	Size of tested samples: Control group	Specimen	Antigen or antibody types	Sensitivity/Specificity	Reference
				90.9 % IgG antibodies specificity Up to 90% IgG antibodies positive rate positive rate before and after conversion to SARS-cov2- virus-negative.	
Enzyme-linked immunosorbent assay (ELISA) (China)	212:100	Serum	Recombinant nucleocapsid protein (N protein)	68.2% IgM positive rate 70.1% IgG positive rate 80.4% IgM and/or IgG positive rate Specificity not described.	[33]
			Recombinant spike protein (S protein)	77.1% IgM positive rate 74.3 IgG positive rate 82.2% IgM and/or IgG positive rate Specificity (N.D.)	
Rapid and sensitive lateral flow immunoassay (LFIA) (China)	7:51	Serum	Recombinant nucleocapsid phosphoprotein gene	100% sensitivity 100% specificity The cutoff value was 0.0666	[34]
Field-effect transistor (FET)-based biosensing device Rapid Antigen Test (Korea)	N.D.	Nasopharyngeal swab	Anti-SARS-CoV-2 spike protein antibody-coated graphene sheets	Medium [LOD]: 1.6×10^1 pfu/mL Clinical sample LOD: 2.42×10^2 copies/mL Sensitivity (N.D.) Specificity (N.D.)	[35]

Method/ (Country)	Size of tested samples: Control group	Specimen	Antigen or antibody types	Sensitivity/Specificity	Reference
ELISA/90% plaque reduction neutralization test ($PRNT_{90}$)/ microneutralization (China–USA)	51:200	Serum	Recombinant RNA-binding domain of the SARS-CoV-2 spike protein	Sensitivity (N.D.) Specificity (N.D.)	[36]
Rapid Antigen Test (Belgium)	106 42	Nasopharyngeal swab	Monoclonal antibody conjugated to colloidal gold nanoparticles. COVID-19 Ag Respi-Strip (Coris Bioconcept, Gembloux, Belgium)	30.2% sensitivity 100% specificity	[37]

essays are very specific, they are also associated with a greater probability of false negatives, and negative results cannot exclude the presence of infection. However, results can be verified by RT-PCR [10].

2. CONCLUSION

Early diagnosis and medical intervention are still the best means of avoiding SARS-CoV-2 infection-related complications. Although RT-PCR remains the gold-standard technique for the diagnosis of COVID-19, there are several disadvantages associated with this molecular approach, including its high cost, cumbersomeness, and the relatively long testing turnaround time. RT-LAPM can be an interesting substitute for RT-PCR. Indeed, this molecular method is sensitive, very fast (average turnaround time of 45 minutes) and does not require a pre-extraction of the virus before nucleic acid amplification. Therefore, it is recommend that the RT-LAMP technique can be adopted on large scale for the SARS-CoV-2 identification. Despite their high specificity, speed, and ease of use, antigen tests still lack the necessary sensitivity. They can be used as alternative tests even without sample pretreatment and can be used by medical staff. Serological assays targeting SARS-CoV-2-specific antibody remain unreliable until at least 10 days after the onset of symptoms in COVID-19 patients. This technique can be employed to assess the evolution of the disease or for seroepidemiological studies. IgG ELISA using the recombinant antigen of RBD of the spike protein of SARS-CoV-2 could identify the presence of SARS-CoV-2-specific antibodies in human sera. The half-life of IgG is longer than that of IgM. IgG are recommended as reliable biomarkers.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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