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Short communication

Evaluation of an antigen-based test for hospital point-of-care diagnosis of SARS-CoV-2 infection

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ABSTRACT

Background: An accurate diagnosis is essential to identify and manage SARS-CoV-2 infected patients and implement infection control measures. Although real-time reverse transcription polymerase chain reaction (RT-PCR) is the current recommended laboratory method, several rapid antigen point-of-care tests (POCTs) were developed as frontline testing for SARS-CoV-2 infection diagnosis.

Objectives: The aim of this study was to assess a recently CE-approved POCT, SARS-CoV-2 Ag Test on the LumiraDx™ Platform (LumiraDx GmbH, Cologne, Germany) for the identification of SARS-COV-2 infected subjects at hospital setting.

Methods: LumiraDx POCT was implemented in three hospital settings: adult and pediatric emergency departments and occupational medicine department along two-month period during the second peak of Italian SARS-CoV-2 pandemic. Rapid antigen testing was performed on direct nasal swabs and results were compared with those obtained by Xpert Xpress SARS-CoV-2 assay.

Results: Overall sensitivity, specificity, NPV and PPV were 90.3%, 92.1%, 95.1%, and 84.9%, respectively, compared to reference method. Sensitivity, specificity, PPV and NPV for symptomatic group were 89.3% [95% IC 84.2-93.3], 88.2% [95% IC 72.5-96.7], 97.8% [95% IC 94.6-99.1], and 58.8% [95% IC 48.4-68.5], respectively. Sensitivity, specificity, PPV and NPV for asymptomatic group were 92.1% [95% IC 85-96.5], 92.3% [95% IC 89.9-94.4], 67.9% [95% IC 61.3-73.8], and 98.5% [95% IC 97.1-99.2], respectively. False positive and negative antigen testing results in both symptomatic and asymptomatic group were observed.

Conclusion: SARS-CoV-2 Ag POCT may represent an interesting tool to rapidly identify symptomatic or asymptomatic infected subjects. However, in hospital setting in which false negative or false positive results may have relevant implications, confirmatory NAAT always remains necessary for the appropriate management of patients.

1. Background

The coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a major public health emergency worldwide [1,2]. As the clinical manifestation of SARS-CoV-2 infection is highly variable, from asymptomatic to severe acute respiratory distress syndrome, an accurate diagnosis is crucial to identify and manage infected patients and implement infection control measures to limit SARS-CoV-2 spread. Probe-based real-time reverse transcription polymerase chain reaction (RT-PCR) has been the gold standard method for SARS-CoV-2 detection and widely used for screening, as recommended by WHO and CDC [3,4]. However, RT-PCR as well as the other molecular assays (i.e. loop-mediated isothermal amplification-based assay [RT-LAMP], microarray, and high-throughput sequencing) are costly, often time consuming and require special equipment and skilled laboratory personnel. Furthermore, growing SARS-CoV-2 pandemic and the dearth of molecular testing capacity, as well as reagents around the world, demanded the development of

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point-of-care tests (POCTs) as frontline testing for SARS-CoV-2 infection diagnosis. Antigen-detecting rapid diagnostic tests are relatively inexpensive, simple to perform and enable obtaining point-of-care results within few minutes [5–13].

2. Objective

The aim of this study was to assess a recently CE-approved POCT, SARS-CoV-2 Ag Test on the LumiraDx™ Platform (LumiraDx GmbH, Cologne, Germany) for the identification of SARS-COV-2 infected individuals in comparison with the reference method RT-PCR.

3. Study design

The prospective controlled observational study was conducted at the University Hospital Città della Salute e della Scienza di Torino, Turin (Italy), which is the largest tertiary care facility in Europe. Three hospital settings were considered: adult and pediatric emergency departments and occupational medicine department along the period October 2020 to December 2020, during the second peak of Italian SARS-CoV-2 pandemic.

The LumiraDx™ SARS-CoV-2 Antigen Test is a microfluidic immunofluorescence assay for the direct and qualitative detection of nucleocapsid protein antigen of SARS-CoV-2 in nasal and nasopharyngeal swab specimens. It exploits microfluidic test strips that contain specific antibodies to form an immunoassay complex that uses a fluorescent latex signal to detect the nucleocapsid protein antigen in the test sample. It was performed on direct nasal swabs in the three wards by trained staff according to manufacturer's instructions. In parallel, nasopharyngeal swabs were collected in COPAN's UTM and tested using Xpert Xpress SARS-CoV-2 assay (Cepheid, Sunnyvale, CA) [14] at the Microbiology and Virology Unit within few hours after collection. All participants provided information on demographic characteristics and on the presence of current or past symptoms potentially related to SARS-CoV-2 infection [15].

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the LumiraDx POCT with 95% confidence interval [95% CI] were computed using the free software MedCalc website (http://medcalc.org/).

The RT-PCR Ct values were recorded in cases of RT-PCR positive/antigen testing negative paired results. In the other cases with RT-PCR negative/antigen testing positive, a second nasopharyngeal swab was collected and analyzed by RT-PCR 24h after the first paired swabs collection.

4. Results

Overall, 907 patients were evaluated, including 656 and 165 subjects at the adult and pediatric emergency departments, respectively, and 86 healthcare workers at the occupational medicine unit. The mean age of ~~the~~ study population was 47.9 (range: 2 months-94 years) with a sex ratio of 0.8 (402 male and 505 women). At specimen collection, 676 (74.5%) participants were asymptomatic and 231 (25.5%) reported experiencing one or more COVID-19 symptoms. The median interval from symptom onset to specimen collection was 4 days (interquartile range 2-7).

According to RT-PCR results, 298 (32.9%) participants were positive to SARS-CoV-2, of which 197 (85.3%) and 101 (14.9%) with symptoms and no symptoms, respectively (Table 1).

Performance of LumiraDx POCT was showed in Table 1. Overall sensitivity, specificity, PPV and NPV were 90.3% [95% IC 86.3-93.4], 92.1% [95% IC 89.7-94.1], 84.9% [95% IC 81-88], and 95.1% [95% IC 93.2-96.5], respectively.

Sensitivity, specificity, PPV and NPV for symptomatic group were 89.3% [95% IC 84.2-93.3], 88.2% [95% IC 72.5-96.7], 97.8% [95% IC 94.6-99.1], and 58.8% [95% IC 48.4-68.5], respectively.

Table 1
Performance of SARS-CoV-2 Ag Test on the LumiraDx™ Platform compared to RT-PCR reference method.

Results and Performance	Real-time RT-PCR Positive	Negative	Total
LumiraDx SARS-CoV-2 Ag Test results			
All partecipants			
Positive	29.7 (269)	5.3 (48)	35 (317)
Negative	3.2 (29)	61.8 (561)	65 (590)
Total	32.9 (298)	67.1 (609)	100 (907)
Symptomatic (≥1 symptom)			
Positive	76.2 (176)	1.7 (4)	77.9 (180)
Negative	9.1 (21)	13 (30)	22.1 (51)
Total	85.3 (197)	14.7 (34)	100 (231)
Asymptomatic			
Positive	13.8 (93)	6.5 (44)	20.3 (137)
Negative	1.1 (8)	78.6 (531)	79.7 (539)
Total	14.9 (101)	85.1 (575)	100 (676)
LumiraDx SARS-CoV-2 Ag Test performance, % [95% CI]			
All partecipants (n = 907)			
Sensitivity	90.3 [86.3-93.4]		
Specificity	92.1 [89.7-94.1]		
PPV	84.9 [81-88]		
NPV	95.1 [93.2-96.5]		
Symptomatic (n = 231)			
Sensitivity	89.3 [84.2-93.3]		
Specificity	88.2 [72.5-96.7]		
PPV	97.8 [94.6-99.1]		
NPV	58.8 [48.4-68.5]		
Asymptomatic (n = 676)			
Sensitivity	92.1 [85-96.5]		
Specificity	92.3 [89.9-94.4]		
PPV	67.9 [61.3-73.8]		
NPV	98.5 [97.1-99.2]		

All data are shown as relative,%, and absolute (n) frequencies if not otherwise stated.
Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

Sensitivity, specificity, PPV and NPV for asymptomatic group were 92.1% [95% IC 85-96.5], 92.3% [95% IC 89.9-94.4], 67.9% [95% IC 61.3-73.8], and 98.5% [95% IC 97.1-99.2], respectively. Among RT-PCR positive/antigen testing negative cases, the mean RT-PCR Ct value was 35.4 (range 27.8-40.5).

False positive antigen testing results were observed in both symptomatic and asymptomatic group, 1.7% (n = 4) and 6.5% (n = 44), respectively. None of the patients positive by LumiraDx™ POCT tested positive by molecular testing on the second nasopharyngeal swab collected 24h after. False negative antigen testing results were also observed in both symptomatic and asymptomatic group, 9.1% (n = 21) and 1.1% (n = 8), respectively.

5. Discussion

In the ongoing pandemic context of COVID-19, diagnostic testing for SARS-CoV-2 is crucial to limit the spread of the virus and manage infected patients. Several rapid tests based on SARS-CoV-2 proteins detection have been developed and are now available on the market. Despite rapid antigen tests were reported to have high specificity, a wide range of sensitivity, often lower than declared by the manufacturers, was reported [8–13]. In this evaluation, sensitivity of LumiraDx™ POCT was acceptable (90.3%) when compared to RT-PCR, slightly lower than reported by the manufacturer (93.1%) but significantly higher than most evaluated rapid antigen-based tests [7–13].

However, if considering population tested, in symptomatic group showing a high prevalence of SARS-CoV-2 infection (85.3%), the low NPV suggested that in settings with relatively high SARS-CoV-2 prevalence patients with a negative antigen testing result should require a confirmatory Nucleic Acid Amplification Test (NAAT). Although we did not perform a detailed correlation analysis between RT-PCR Ct values

and antigen testing results, we observed relatively high Ct values in individuals with false-negative antigen testing results, as previously and extensive reported [5-8,10-13].

In asymptomatic group showing a quite lower prevalence of SARS-CoV-2 infection (14.9%), the low PPV suggested that in settings with relatively low SARS-CoV-2 prevalence a confirmatory NAAT testing should be considered for patients with a positive antigen test result. Conversely, the high NPV showed that patients with a negative antigen test result are unlikely to be infected with SARS-CoV-2 and could not require confirmatory NAAT.

Given the relevant number of both false negative and positive results, implementation in hospital settings of SARS-CoV-2 Ag test-based algorithms might outweigh benefits [16], especially in emergency and occupational medicine departments. In fact, management of both symptomatic and asymptomatic patients who need hospitalization for other reasons than COVID-19 would require in any case a confirmatory NAAT, unshortening emergency stay. Similarly, management of healthcare workers should also include a confirmatory NAAT given the relevant impact of both false negative and positive results in term of risk of spreading SARS-CoV-2 in hospital settings and health services disruption for sick leave. In conclusion, although SARS-CoV-2 Ag Test on the LumiraDx™ Platform has important advantages such as rapidity, lower cost, easy-to-use, limited technical skill and equipment required in comparison to molecular testing, our data highlighted relevant limitations in PPV and NPV. Analytical performance of rapid antigen testing largely depends on several factors, such as viral load, quality of the specimen and processing methods, time from symptoms onset and setting of patients tested. Therefore, SARS-CoV-2 Ag POCT may represent an interesting tool to rapidly identify symptomatic or asymptomatic infected individuals and its adoption might be more suitable in mass screening programs, with confirmatory NAAT of individuals tested positive. Conversely, in setting in which false negative or false positive results may have relevant implications, confirmatory NAAT always remains necessary for the appropriate management of patients.

Authors Declarations

All named authors have seen and agreed to the submitted version of the paper; all who are included in the acknowledgements section, or as providers of personal communications, have agreed to those inclusions; the material is original, unpublished and has not been submitted elsewhere.

- No material which has been published elsewhere is contained in the article.
- No material related to commercial products is contained in the article.
- No pending publication of the material in conference proceedings, letters to journals and brief communications etc. is contained in the article.
- All authors declare no conflict of interest and no sources of funding.
- The authors received no financial support for the research.
- The study was performed according to the declaration of Helsinki principles and our institution's ethical standards.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

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