Peer Review File

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Reviewer A

The research is innovative; it could represent a useful tool for healthcare workers who deal with the execution of the pharyngeal swabs.

Comment1: In my opinion, the authors performed a diagnostic study which could be implemented by a better definition of the study design, according to the international guidelines.

Reply 1: We agree with these valuable suggestions that the referee put forward. However, the feasibility of a more optimal study was limited by the timing and study sites. When this study was conducted, there were barely new confirmed COVID-19 cases in Wuhan; we couldn't implement the diagnostic study by a better definition in our hospital. The main limitations were pointed out (Page 18, line 14-20) in the manuscript and we believed that the device and ideas we designed can be testified well by the medical institutions in other epidemic areas.

Changes in the text: A limitation of our study was the relatively small number of participants included in the efficacy test…we have created can be tested and further validated by medical institutions in other epidemic areas.

Comment 2: They proposed the use of a diagnostic tool to perform pharyngeal swab and compared the diagnostic performance with a reference standard, i.e., the traditional pharyngeal swab. Additional information should be provided as regards methods of recruitment, time between index and reference test, statistical analysis, etc.

Reply 2: Thanks for these valuable suggestions. We added up the methods of recruitment (Page 9, line 19 to page 10, line 6) and results of agreement statistics such

as Kappa co-efficient (Page 12, line 5-8) in the manuscript. The time (date of procedure) between index and reference test was already documented in Table S1 in the first version of manuscript.

Changes in the text:

Methods of recruitment: A self-controlled case series (SCCS) study method was used to evaluate the accuracy of the RT-PCR results obtained from optimized pharyngeal swab samples from patients who had been confirmed to be actively COVID-19 positive according to WHO interim guidance (Fig. 1). All patients included in the trial returned at least one positive test result within a week before their recruitment at Wuhan Union Hospital. The exclusion criteria for our study were: 1) maxillofacial deformities or related underlying diseases; 2) an interincisor distance of less than three transverse fingers; 3) dentition defects and edentulous patients; 4) critical illness; or (5) inability to comply with the pharyngeal swab.

Results of agreement statistics: The McNemar test and the kappa statistic were conducted to test the significance of the difference between the efficacies of the two diagnostic procedures. A P-value < 0.05 was regarded as being statistically significant.

Reviewer B

Authors describe use of OPAD in an attempt to reduce exposure and optimize screening for COVID-19.

Major Comments:

Comment 1: “In Italy, medical professionals have been working since the end of February, and around 20% (n=350) of them have become infected, even have died”. Unsure about the accuracy of this statement. Please provide references for this.

Reply 1: We apologize for the negligence in the manuscript. In fact, the data came from an article on the Journal ‘The Lancet’ (DOI:https://doi.org/10.1016/S0140-6736 (20)30627-9). As more than two months have passed, we updated the epidemiological

data in the revised manuscript. (See Page 6, line 4-18)

Changes in the text: As of July 20, 2020, the World Health Organization (WHO) had documented 14,263,202 confirmed cases and 602,244 deaths globally (https://www.who.int./) ..., a number of studies have reported the prevalence of SARS-CoV-2 infection among healthcare workers in other parts of the world.

Comment 2: Figure A is redundant and difficult to interpret, can be completely removed from the manuscript.

Reply 2: Do you mean the Figure 2A? We performed the questionnaire to obtain eligible responsive healthcare workers from the frontline during COVID-2 pandemics. The results raised the problem that the insufficient exposure of operation fields and the fears of virus infection may compromise the accuracy of RT-PCR of pharyngeal sampling; therefore, we thought it was necessary to present the survey results. If you have other concerns, please do not hesitate to discuss with us.

Comment 3: Most of the patients (77%) described in this study had Mallampati score of 1 which makes it easier for the automated OPAD to carry out the procedure of collected swab sample. This point towards a selection bias. Authors should mention this as one of the limitation.

Reply 3: Thank you for the valuable advice. Yes, the better MS score in this cohort pointed towards a selection bias, and we mention this in discussion of the revised manuscript. (see Page 18, line 17-20)

Changes in the text: Another drawback is that most of the patients (77%) enrolled in this study had an MS of 1 which indicates a selection bias; however, we believe that the device and ideas we have created can be tested and further validated by medical institutions in other epidemic areas.

Comment 4: If possible authors should present a subgroup analysis comparing the efficacy of OPAD versus conventional method for obtaining swab samples based on the mallampati score (especially in group 2 and above).

Reply 4: Thank you for raising this critical issue, this really highlight the value of the OPAD in the patients with higher MS. As there only four patients with MS 2 and one with MS 3, the statistics comparison in subgroup may be inaccurate. Still, we calculated the positive rate of OPAD and conventional method in a subgroup analysis. The results showed that OPAD may show a better sensitivity (positive rate) in the patients with higher MS scores.

Efficacy of OPAD versus traditional method for swab sampling

MS_Score			OPAD		
			negative	positive	Total
1	Traditional	negative	7(41.1)	1(5.9)	8(47.06)
		positive	1(5.9)	8(47.06)	9(53.94)
	Total		8(47.06)	9(53.94)	17
2-3	Traditional	negative	2(40)	2(40)	4(80)
		positive	0(0)	1(20)	1(20)
	Total		2(40)	3(60)	5
Total	Traditional	negative	9(40.91)	3(13.64)	12(54.55)
		positive	1(4.55)	9(40.91)	10(45.45)
	Total		10(45.45)	12(54.55)	22

Note: Data were presented as count (percentage of total)

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			negative	positive	Total
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	Total		8(47.06)	9(53.94)	17
2	Traditional	negative	2(50)	1(25)	3(75)
		positive	0(0)	1(25)	1(25)
	Total		2(50)	2(50)	4
3	Traditional	negative	N	1(100)	1(100)

	Total	N	1(100)	1
Total	**Traditional negative**	9(40.91)	3(13.64)	12(54.55)
	positive	1(4.55)	9(40.91)	10(45.45)
	Total	10(45.45)	12(54.55)	22

Note: Data were presented as count (percentage of total)

Changes in the text: see page 16, line 1 and page 18, line 11; besides, we have added a new table, Table 3;

Revised text: 1) Moreover, the efficacy of OPAD was evaluated in a subgroup analysis based on MS. Of the five patients with higher MS (MS=2-3), four (80%) had a positive diagnosis using OPAD, while only one (20%) was positive using the traditional method (Table 3).

2) The OPAD keeps the patient's mouth open and tongue pressed down simultaneously, which means the healthcare worker can avoid close exposure and be less anxious while performing the procedure. This may also improve the accuracy of swab sampling, especially for patients with higher MS scores, and has great significance for the diagnosis and recovery assessment of COVID-19 patients.

Comment 5: Although authors claim that the use of device will reduce the use of PPE equipment and to a level it may be true. However, since the device is not completely automated, it will need a person operating the device and to confirm appropriate sample collection (and the operator will require PPE as well).

Reply 5: As the conventional throat swab can generate aerosol particles and needs near-distance operation, the occupational exposure risk for healthcare worker is thought to be similar to the risk of incubation (Doi: https://doi.org/10.1007/s12630-020-01591-x). Although the OPAD is not completely automated, the distance between the operator and patients is parallel to a routine medical operation, such as intravenous injection, or blood pressure measuring, leading us to believe that OPAD can lower the prevention level. This advice should be a compensation for the insufficient protection, as not all the countries have enough

PPEs.

Comment 6:

Statistical analysis: Authors should describe the results while comparing the sampling done by OPAD or by conventional method using the agreement statistics such as Kappa co-efficient for agreement or disagreement for positive and negative testing between the two groups.

Authors should also provide an ROC curve for the sensitivity and specificity for using the test by OPAD versus the traditional method of collecting swab samples.

Reply 6: Sorry for the neglect, we have made the corresponding changes for statistical analysis: 1) Kappa co-efficient between the two sampling methods was added to test the consistency of the two diagnostic procedures efficacy (See page 12, line 508 and page 15, line 9-11).

Changes in the text: 1) The McNemar test and the kappa statistic were conducted to test the significance of the difference between the efficacies of the two diagnostic procedures. A P-value < 0.05 was regarded as being statistically significant. 2) The kappa coefficient between the two methods was 0.639 ($P = 0.002$), which meant that the similarities between two diagnostic methods were significant, albeit moderately.

2) ROC Curves for Correlation of OPAD with the traditional method of collecting swab samples (served as the Gold Standard, see Page 15, line 14) was also added in Fig.3C

Changes in the text: The ROC analysis for the sensitivity and specificity of using the OPAD versus the traditional method also indicated that the OPAD showed good efficacy in pharyngeal sampling for COVID-19 patients (Fig. 3C, AUC = 0.825).