Received: 15 March 2021 | Revised: 9 April 2021 | Accepted: 13 April 2021

DOI: 10.1002/jmv.27026

RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

Comparison of saliva with oral and nasopharyngeal swabs for SARS-CoV-2 detection on various commercial and laboratory-developed assays

Annie-Claude Labbé[1,2,3] | Patrick Benoit[2] | Sarah Gobeille Paré[4] | François Coutlée[2,3] | Simon Lévesque[5,6] | Julie Bestman-Smith[4] | Jeannot Dumaresq[7] | Christian Lavallée[1,2,3] | Claudia Houle[8] | Philippe Martin[5,6] | Anton Mak[9] | Philippe Gervais[10] | Stéphanie Langevin[11,3] | Mariève Jacob-Wagner[4] | Simon Gagnon[2,3] | Manon St-Hilaire[3] | Nathalie Lussier[9] | Ariane Yechouron[11,3] | David Roy[12] | Michel Roger[2,3,12] | Judith Fafard[12]

[1]Service de maladies infectieuses et de microbiologie, Département de médecine spécialisée, Hôpital Maisonneuve-Rosemont - CIUSSS de l'Est-de-l'Ile-de-Montréal, Montréal, Québec, Canada

[2]Département de microbiologie, infectiologie et immunologie, Université de Montréal, Montréal, Québec, Canada

[3]Département clinique de médecine de laboratoire, Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada

[4]Service de microbiologie-infectiologie, Centre Hospitalier Universitaire de Québec – Université Laval, Québec, Québec, Canada

[5]Service de microbiologie, Centre Hospitalier Universitaire de Sherbrooke - CIUSSS de l'Estrie, Sherbrooke, Québec, Canada

[6]Département de microbiologie et infectiologie, Université de Sherbrooke, Sherbrooke, Québec, Canada

[7]Département des laboratoires, Hôpital Hôtel-Dieu de Lévis - CISSS de Chaudière-Appalaches, Lévis, Québec, Canada

[8]Service de microbiologie-infectiologie, Département de médecine spécialisée, Centre hospitalier affilié universitaire régional - CISSS de la Mauricie-Centre-du-Québec, Trois-Rivières, Québec, Canada

[9]Département de médecine de laboratoire, Hôpital Charles Lemoyne - CISSS Montérégie-Centre, Greenfield Park, Québec, Canada

[10]Département des laboratoires, Institut Universitaire de Cardiologie et de Pneumologie de Québec, Québec, Québec, Canada

[11]Service de microbiologie-infectiologie, Département de médecine spécialisée, CIUSSS du Centre-Sud de Montréal, Montréal, Québec, Canada

[12]Laboratoire de Santé Publique du Québec, Institut national de santé publique du Québec, Ste-Anne-de-Bellevue, Québec, Canada

Correspondence
Annie-Claude Labbé, Département de microbiologie et d'infectiologie, Hôpital Maisonneuve-Rosemont, 5415, Blvd. de l'Assomption, Montréal, Québec, H1T 2M4, Canada.
Email: ac.labbe@umontreal.ca

Abstract

The accurate laboratory detection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a crucial element in the fight against coronavirus disease 2019 (COVID-19). Reverse transcription-polymerase chain reaction testing on combined oral and nasopharyngeal swab (ONPS) suffers from several limitations, including the need for qualified personnel, the discomfort caused by invasive nasopharyngeal sample collection, and the possibility of swab and transport media shortage. Testing on saliva would represent an advancement. The aim of this study was to compare the concordance between saliva samples and ONPS for the detection of SARS-CoV-2 on various commercial and laboratory-developed tests (LDT). Individuals were recruited from eight institutions in Quebec, Canada, if they

had SARS-CoV-2 RNA detected on a recently collected ONPS, and accepted to provide another ONPS, paired with saliva. Assays available in the different laboratories (Abbott RealTime SARS-CoV-2, Cobas® SARS-CoV-2, Simplexa™ COVID-19 Direct, Allplex™ 2019-nCoV, RIDA®GENE SARS-CoV-2, and an LDT preceded by three different extraction methods) were used to determine the concordance between saliva and ONPS results. Overall, 320 tests were run from a total of 125 saliva and ONPS sample pairs. All assays yielded similar sensitivity when saliva was compared to ONPS, with the exception of one LDT (67% vs. 93%). The mean difference in cycle threshold (ΔC_t) was generally (but not significantly) in favor of the ONPS for all nucleic acid amplification tests. The maximum mean ΔC_t was 2.0, while individual ΔC_t varied importantly from −17.5 to 12.4. Saliva seems to be associated with sensitivity similar to ONPS for the detection of SARS-CoV-2 by various assays.

KEYWORDS

epidemiology, pandemics, research and analysis methods, RNA extraction, SARS coronavirus, virus classification

1 | INTRODUCTION

Strategies for the prevention of transmission and treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rely on accurate and timely diagnosis of the infection. The gold standard for the diagnosis of coronavirus disease 2019 (COVID-19) from the outset of the pandemic has been a reverse transcription-polymerase chain reaction (RT-PCR) test on a combined oral and nasopharyngeal swab (ONPS). ONPS is considered to have the highest sensitivity but suffers from several limitations.[1] First, a trained professional is required to obtain a specimen, which represents a substantial strain on human resources and poses a risk of infection transmission. Second, flocked swabs and transport media are prone to shortages in the context of the high number of tests. Third, this invasive sample collection is associated with significant discomfort which may impact on acceptability, particularly in repeated screening settings. This has motivated the search for new specimens, such as saliva, that yield acceptable results on commercial platforms and laboratory-developed tests (LDTs).

Salivary specimens have the advantage of being easily self-collected and more acceptable by the patient than an ONPS.[2,3] A recent meta-analysis of 16 pooled studies using different protocols showed a similar sensitivity for SARS-CoV-2 detection when saliva and nasopharyngeal swab (NPS) specimens were compared.[4] Large unpooled studies are required to confirm these findings. Since most studies have been conducted using varying testing platforms, it remains unknown whether a specific nucleic acid amplification test (NAAT) protocol is more suitable for saliva than others.

The *Laboratoire de Santé Publique du Québec* (LSPQ), a provincial public health laboratory, therefore undertook a multicentric study in eight hospital laboratories to compare saliva samples to ONPS for SARS-CoV-2 detection. A secondary objective was to compare the difference in cycle threshold (C_t) values between saliva and ONPS samples.

2 | MATERIALS AND METHODS

This multicentric study was conducted in the Centre hospitalier universitaire de Québec, Centre hospitalier universitaire de Montréal, Centre hospitalier universitaire de Sherbrooke, Centre hospitalier régional de Trois-Rivières, Hôpital Charles-Lemoyne, Hôpital Maisonneuve-Rosemont, Hôtel-Dieu de Lévis, Institut universitaire de cardiologie et de pneumologie de Québec, and LSPQ.

Individuals were eligible if they were ≥18 years old, and had SARS-CoV-2 RNA detected from an ONPS recently collected using a NAAT method. They were recruited between May 12, 2020 and June 25, 2020, if they accepted to provide another ONPS at the same time of a saliva sample. The time elapsed between the first positive test and the inclusion in the study was not recorded.

This study was approved by the Provincial Public Health Authority and was conducted following the principles set out in the Helsinki Accord. Free and informed consent was obtained from the subjects. Samples were anonymized to maintain the confidentiality of participants and their utilization was restricted to SARS-CoV-2 nucleic acid detection only. Demographic characteristics and clinical information of participants were not collected.

2.1 | Sample collection

Saliva was collected before ONPS samples at the same visit. Subjects were told to avoid smoking, drinking, eating, brushing teeth, or

chewing gum at least 30 min before sample collection. Saliva samples were collected into 50 ml conical Falcon tubes or in 80 ml sterile plastic urine containers. Participants were instructed to spit repeatedly until 2–10 ml of saliva was obtained.

The ONPS was obtained by first sampling the oropharynx with a flocked swab and then the nasopharynx by inserting the same swab in the nostril to reach the nasopharyngeal cavity and rotating it a few times. Flocked swabs were placed into one of the following transport media: Modified Hanks Balanced Salt Solution, molecular biology grade water, or 0.9% saline.

All samples were sent to one of the eight participant laboratories on icepacks, where they were refrigerated between 2°C and 8°C until processing.

2.2 | Sample processing and nucleic acid extraction

Saliva and ONPS were tested in parallel in the aforementioned laboratories using in-house or commercial SARS-CoV-2 NAAT. Since some laboratories had more than one platform, the 125 specimen pairs were tested with up to four different NAATs, for a total of 320 distinct tests. The volume of saliva was recorded and, when sufficient volume was available (n = 24), 1 ml of saliva was aliquoted to test the undiluted sample in parallel with the diluted sample which was processed as follows: An equal volume of molecular biology grade water was mixed with the remaining saliva sample (dilution 1:1) to decrease the viscosity. All saliva samples (undiluted and diluted) were vortexed using biosafety work practices and when deemed required by the technician, highly viscous saliva samples were centrifuged before pipetting. ONPS were tested without vortexing nor centrifugation.

The different commercially available assays were: (a) Simplexa™ COVID-19 Direct Kit (DiaSorin Molecular LLC); (b) Abbott RealTime SARS-CoV-2 assay performed on the Abbott m2000 RealTime system (Abbott Molecular); (c) Cobas® SARS-CoV-2 performed with the Cobas®6800 system (Roche); (d) Allplex™ 2019-nCoV assay with thermal lysis (Seegene), and (e) RIDA®-GENE SARS-CoV-2 test (R-Biopharm) using BD MAX™ ExK TNA-2 and TNA-3 Nucleic Acid Isolation Kit (Becton Dickinson). A LDT was performed on the LightCycler® 480 Instrument II (Roche) or the QuantStudio™ 6 Pro Real-Time PCR System (Applied Biosystems™) after thermal lysis or chemical extraction of RNA using NucliSens easyMAG platform (bioMérieux) or the Magna Pure platform or the Cobas® 4800 system (Roche) as previously described.[5] For thermal lysis, 20–25 µl of the sample was diluted 1:1 in molecular grade water, heated at 90°C for 2 min and then cooled to 4°C for 3 min. Five microlitres were taken directly as a template for RT-PCR (LSPQ in-house protocol). None of the specimens were inactivated with an external lysis buffer before being processed on any of the platforms mentioned.

2.3 | SARS-CoV-2 nucleic acid detection by RT-PCR

Diagnostics of SARS-CoV-2 viral infection were conducted based on an RT-PCR approach. All procedures were conducted according to the different manufacturer's recommendations. RT-PCR targets are listed in Table 1.

2.4 | Data and statistical analyses

All recruited individuals (n = 125) had at least one positive NAAT result either on saliva or ONPS. Thus, in the calculations of specimen performance, all individuals were considered to be SARS-CoV-2 positive. The sensitivity of assays and concordance between assays was calculated with a 95% confidence interval. Differences in continuous variables were assessed using the two-sample Wilcoxon rank-sum (Mann–Whitney) test. Statistical analyses were done using STATA v16.1 (College Station).

TABLE 1 Characteristics of commercial and laboratory-developed tests for SARS-CoV-2 detection

Assay	Extraction	Amplification and detection	Target gene(s)
Simplexa™ COVID-19 Direct	Integrated	LIAISON® MDX system	ORF1ab, S
Abbott RealTime SARS-CoV-2	Abbott m2000 RealTime system		RdRp, N
Cobas® SARS-CoV-2	Cobas®6800 system		ORF1ab, E
Allplex™ 2019-nCoV	Thermal lysis	CFX96 Touch™	RdRp, E, N
RIDA®GENE SARS-CoV-2	BD MAX™ ExK TNA-2 and TNA-3	BD MAX™ system	E
RT-PCR LDT	NucliSens easyMAG platform	LightCycler® 480 Instrument II	E
		QuantStudio™ 6 Pro	
	Cobas®4800 system	LightCycler® 480 Instrument II	
	Thermal lysis	LightCycler® 480 Instrument II	

Abbreviations: COVID-19, coronavirus disease 2019; LDT, laboratory-developed test; RT-PCR, reverse-transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

3 | RESULTS

A total of 125 saliva and ONPS sample pairs were included in the study. Twenty-five pairs (20%) were tested by only one platform; the other pairs were tested by two (32; 26%), by three (45; 36%), or by four (23; 18%) different platforms, for a total of 320 paired test results. The volume of saliva was recorded for 66/125 samples: mean volume was 3.2 ml (median: 3 ml, interquartile range: 1–5 ml). The saliva volume was particularly small when collected from the 10 participants in long-term care facilities (median: 1 ml). Laboratory technicians reported pipetting difficulties related to the viscosity of saliva specimens even when diluted, leading to invalid results. All initially invalid tests had to be repeated, increasing workload (after repeat testing, however, only 4/320 final invalid results were reported).

The sensitivity of ONPS and saliva samples with different platforms is shown in Table 2. Commercial assays yielded similar sensitivity when saliva was compared to ONPS. The LDT combined with RNA extraction using the NucliSens easyMAG platform performed poorly (66.7% vs. 92.7%; $p < 0.001$). The observed difference in sensitivity using the Abbott RealTime SARS-CoV-2 assay (75.0% vs. 95.2%) is not statistically significant. Among the 10 pairs yielding discordant results (saliva negative/ONPS positive), nine were tested with another platform and only one saliva sample was positive; the eight other saliva samples remained negative on the other platform.

The secondary objective of the study was to compare C_t in both specimen types. The mean difference in C_t when NAAT was positive for both samples was slightly (but not significantly) in favor of the ONPS for all NAATs, except for LDT with RNA extraction with the Cobas® 4800 (Table 2). The maximum mean ΔC_t was 2.0, while individual ΔC_t varied importantly from −17.5 to 12.4. When discordant results were analyzed (ONPS was positive and saliva negative), the mean C_t on ONPS tended to be higher than when both results were found to be positive (Table 3). Those mean C_t differences were statistically significant for the Abbott RealTime SARS-CoV-2 assay (24.8 vs. 17.1; $p = 0.01$), Simplexa® COVID-19 Direct Kit (31 vs. 24.2; $p = 0.03$), LDT with RNA combined with the NucliSens easyMAG (32.7 vs. 25.7; $p < 0.001$) and LDT with thermal lysis (34.1 vs. 29.5; $p = 0.01$).

In addition to the 320 NAATs performed on diluted saliva, 41 NAATs (from 24 distinct samples) were performed on undiluted saliva. Results were identical (33 were positive and 8 were negative) whether saliva was tested diluted or undiluted. Among positive samples, the C_t difference between undiluted saliva and diluted saliva ranged from −1.8 to 3.8 (mean: −0.7).

TABLE 2 Sensitivity and C_t differences between saliva and ONPS on different tests protocol ($n = 320$)

Method	Saliva	Oral and nasopharyngeal swabs (ONPS)		Sensitivity % (95% CI)		C_t difference when NAAT is positive on both samples[a]
		Negative	Positive	Saliva	ONPS	Mean (range)
Simplexa® COVID-19 Direct Kit ($n = 49$)	Negative	NA	4	91.8 (79.8–97.0)	83.7 (70.2–91.8)	1.2 (−7.4–11.7)
	Positive	8	37			
Abbott RealTime SARS-CoV-2 assay ($n = 40$)[b]	Negative	NA	10	75.0 (58.9–86.3)	95.2 (82.2–98.9)	0.1 (−11.4–10.3)
	Positive	2	28			
Cobas® SARS-CoV-2 test ($n = 17$)	Negative	NA	2	88.2 (60.3–97.4)	88.2 (60.3–97.4)	0.8 (−9.5–4.9)
	Positive	2	13			
Allplex™ 2019-nCoV assay ($n = 27$)	Negative	NA	2	92.6 (73.4–98.3)	88.9 (69.4–96.6)	1.5 (−9.4–7.4)
	Positive	3	22			
RIDA®GENE SARS-CoV-2 test using BD MAX™ Isolation Kit ($n = 39$)[b]	Negative	NA	1	96.8 (79.0–99.6)	82.1 (66.3–91.4)	2.0 (−12.3–12.4)
	Positive	7	31			
LDT/Cobas 4800 system ($n = 29$)	Negative	NA	0	100 (83.2–100)	69.0 (49.4–83.5)	−0.1 (−5.9–7.8)
	Positive	9	20			
LDT/NucliSens easyMAG platform ($n = 55$)	Negative	NA	17	66.7 (52.7–78.4)	92.7 (81.8–97.3)	1.3 (−17.5–10.7)
	Positive	4	34			
LDT/thermal lysis ($n = 60$)	Negative	NA	7	88.3 (77.2–94.4)	83.3 (71.4–90.9)	0.1 (−15.8–12.4)
	Positive	10	43			

Abbreviations: C_t, cycle threshold; CI, confidence interval; LDT, laboratory-developed tests; n, number of samples; NA, not applicable; ONPS, oral and nasopharyngeal swab.

[a]C_t result on saliva sample − C_t result on ONPS sample (a positive value indicates a stronger signal on the ONPS).

[b]Four invalid results were obtained on saliva samples with Abbott RealTime SARS-CoV-2 assay ($n = 2$) and RIDA®GENE SARS-CoV-2 test using BD MAX™ Isolation Kit ($n = 2$).

TABLE 3 ONPS mean C_t with each assay according to the NAATS result obtained for saliva when ONPS was positive ($n = 271$)

Method	Saliva result	*n*	ONPS mean C_t	Range	*p* Value[a]
Abbott RealTime SARS-CoV-2 assay ($n = 38$)	−	10	24.8	21.3–28.3	0.01
	+	28	17.1	14.1–20.2	
Cobas® SARS-CoV-2 test ($n = 15$)	−	2	33.4	31.3–35.4	NS
	+	13	28.3	24.9–31.7	
Allplex™ 2019-nCoV assay ($n = 24$)	−	2	30.2	−28.0–88.4	NS
	+	22	28.4	26.3–30.5	
Simplexa® COVID-19 Direct Kit ($n = 41$)	−	4	31.0	27.7–34.2	0.03
	+	37	24.2	22.3–26.1	
RIDA®GENE SARS-CoV-2 test using BD MAX™ Isolation Kit ($n = 32$)	−	1	35.5	NA	NS
	+	31	26.7	24.4–29.0	
LDT/Cobas 4800 system ($n = 20$)	−	0	NA	NA	NA
	+	20	30.0	28.3–31.8	
LDT/NucliSens easyMAG platform ($n = 51$)	−	17	32.7	31.6–33.7	<0.001
	+	34	25.7	23.8–27.6	
LDT/thermal lysis ($n = 50$)	−	7	34.1	30.0–38.2	0.01
	+	43	29.5	28.0–31.0	

Abbreviations: C_t, cycle threshold; 95% CI, 95% confidence interval; LDT, laboratory-developed tests; ONPS, oral and nasopharyngeal swab; NA, not applicable; NAAT, nucleic acid amplification test; NS, not significant; *n*, number of samples; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; +, detected; −, not detected.

[a]Two-sample Wilcoxon rank-sum (Mann–Whitney) test.

4 | DISCUSSION

With a sample size bigger than many studies published to date, and a variety of NAATs, the present study contributes to clarifying the performance of saliva as a specimen for SARS-CoV-2 detection.

This study includes a relatively large number of positive SARS-CoV-2 samples with very simple collection instructions and minimal laboratory manipulation. Although we found a nonsignificant trend toward a higher sensitivity of the ONPS, our study confirms that saliva samples have a sensitivity similar to ONPS when infection with SARS-CoV-2 is defined as a participant with at least one positive sample (saliva or ONPS) on at least one NAAT. However, low statistical power due to small numbers of samples may hinder statistically significant differences. The LDT with NucliSens easyMAG RNA extraction showed statistically significant lower sensitivity with saliva, while the LDT with extraction using the Cobas 4800 system or the thermal lysis protocol generated concordant results for ONPS and saliva samples. The difference could be explained in part by the relatively low number of individual tests performed with each NAAT.

When a sample was tested on different platforms, the concordance was high, as only eight saliva samples (6.4%) were found to be discordant (data not shown). As reported by Barat et al.,[6] individuals with a false negative result on saliva samples were associated with a higher C_t value on ONPS. As higher C_t values are associated with lower viral loads, as occurs with resolved infections, the public health and clinical consequences of a false-negative result in this context would probably be diminished.[7] High C_t values can also occur when a person is tested early in the disease course (and therefore infectious); to lessen the consequences of a false-negative result,[8] it is crucial to consider the epidemiological and clinical contexts. When clinical suspicion remains high despite a negative saliva result, asking for an ONPS, in addition, to repeat a saliva sampling, should be considered.

A recent meta-analysis of 16 studies reported a pooled sensitivity of 83.2% for detection of SARS-CoV-2 on saliva, which was evaluated as being similar to the sensitivity of ONPS. However, the authors argued that studies were heterogeneous in their patient selection and their testing methods. Many studies reported a higher C_t on saliva samples, suggesting a lower viral load in this type of specimen.[6,7,9] Another meta-analysis found a higher viral load in NPS samples compared to saliva.[10] This is in contradiction with other studies that found saliva being positive for a longer period and more sensitive than ONPS for the detection of SARS-CoV-2.[11,12]

This study has several limitations. First, the heterogeneity of the population and methods utilized do not allow individual assessment of each technology. Second, the recruitment of patients with an ONPS-confirmed diagnosis may lead to an underestimation of the sensitivity of saliva since the inclusion of participants was based on the ONPS test result and not saliva: individuals who would have tested positive only in saliva initially and not ONPS would not have been recruited in our study. Moreover, some centers might have recruited more remote infections, as suggested by the distribution of the C_t values between centers. The delay after the diagnosis in which the samples were obtained, and other clinical data, were also not recorded and could have adversely affected the sensitivity of saliva samples. In one study with paired nasopharyngeal and saliva samples, a higher percentage of NPS samples than saliva samples was positive when collected 11 days and more after the diagnosis.[12] More data related to the viral load kinetic and detection of SARS-CoV-2 in saliva over time are needed to assess the sensitivity of this specimen in early and late infections. Unfortunately, this analysis is not possible with our data since we did not record the time elapsed between the first positive sample at diagnosis and the recruitment in the study, and the duration of the symptoms at the time of the tests. As clinical information was not recorded in our study, it is impossible to assess if saliva samples are suitable for individual populations such as asymptomatic, ambulatory, or hospitalized individuals.

Many samples showed low volumes (<1 ml) which may be explained by spitting limitations (data not shown). In addition, pipetting difficulties were related to the viscosity of saliva specimens. A promising avenue to overcome these challenges could be to use specimens obtained by gargling, which are already diluted and easy to

collect and manipulate.[13] Future studies will assess if this type of specimen is easier to process and if sensitivity is decreased by diluting saliva in water.

5 | CONCLUSION

This study shows that saliva is a suitable sample for the detection of SARS-CoV-2 by RT-PCR, with a similar sensitivity to ONPS on multiple available assays. The nonstatistically significant trend toward a higher sensitivity of the ONPS was driven by some false-negative results on saliva samples when high C_t was obtained on ONPS paired samples. The clinical consequences of a false negative result in a low viral load infection are still unclear.

ACKNOWLEDGMENTS

The authors are thankful to all study participants and laboratory technicians.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Annie-Claude Labbé: Conceptualization, methodology, formal analysis, statistical analysis, writing – original draft. **Patrick Benoit**: Data interpretation, writing – original draft. **Sarah Gobeille Paré**: Investigation, data interpretation, writing – original draft. **François Coutlée**: Conceptualization, methodology, data interpretation, writing – review and editing. **Simon Lévesque**: Data interpretation, writing – review and editing. **Julie Bestman-Smith**: Conceptualization, methodology, writing – review and editing. **Jeannot Dumaresq**: Conceptualization, methodology, writing – review and editing. **Christian Lavallée**: Formal Analysis, statistical analysis, writing – review and editing. **Claudia Houle, Philippe Martin, Anton Mak, Philippe Gervais, Stéphanie Langevin, Mariève Jacob-Wagner, Simon Gagnon, Manon St-Hilaire, Nathalie Lussier, Ariane Yechouron**: Investigation, formal analysis, writing – review and editing. **David Roy**: Data interpretation, writing – original draft. **Michel Roger**: Project administration, writing – review and editing. **Judith Fafard**: Conceptualization, methodology, data curation, formal analysis, data interpretation, writing – review and editing, supervision.

ORCID

Annie-Claude Labbé https://orcid.org/0000-0001-8936-3307
François Coutlée https://orcid.org/0000-0002-2025-8928

REFERENCES

1. Chen JH, Yip CC, Poon RW, et al. Evaluating the use of posterior oropharyngeal saliva in a point-of-care assay for the detection of SARS-CoV-2. *Emerg Microbes Infect*. 2020;9(1):1356-1359.
2. Azzi L, Carcano G, Gianfagna F, et al. Saliva is a reliable tool to detect SARS-CoV-2. *J Infect*. 2020;81(1):e45-e50.
3. Xu R, Cui B, Duan X, Zhang P, Zhou X, Yuan Q. Saliva: potential diagnostic value and transmission of 2019-nCoV. *Int J Oral Sci*. 2020;12:11.
4. Butler-Laporte G, Lawandi A, Schiller I, et al. Comparison of saliva and nasopharyngeal swab nucleic acid amplification testing for detection of SARS-CoV-2: a systematic review and meta-analysis. *JAMA Intern Med*. 2021;181:353-360.
5. Boutin CA, Grandjean-Lapierre S, Gagnon S, et al. Comparison of SARS-CoV-2 detection from combined nasopharyngeal/oropharyngeal swab samples by a laboratory-developed real-time RT-PCR test and the Roche SARS-CoV-2 assay on a cobas 8800 instrument. *J Clin Virol*. 2020;132:104615.
6. Barat B, Das S, de Giorgi V, et al. Pooled saliva specimens for SARS-CoV-2 testing. *J Clin Microbiol*. 2020;59:e02486-20.
7. Jefferson T, Spencer EA, Brassey J, Heneghan C. Viral cultures for COVID-19 infectious potential assessment - a systematic review [published online ahead of print December 3, 2020]. *Clin Infect Dis*. 2020:ciaa1764. https://doi.org/10.1093/cid/ciaa1764
8. Tom MR, Mina MJ. To interpret the SARS-CoV-2 test, consider the cycle threshold value. *Clin Infect Dis*. 2020;71:2252-2254.
9. Procop GW, Shrestha NK, Vogel S, et al. A direct comparison of enhanced saliva to nasopharyngeal swab for the detection of SARS-CoV-2 in symptomatic patients. *J Clin Microbiol*. 2020;58(11):e01946-20.
10. Czumbel LM, Kiss S, Farkas N, et al. Saliva as a candidate for COVID-19 diagnostic testing: a meta-analysis. *Front Med*. 2020;7:465.
11. Rao M, Rashid FA, Sabri F, et al. Comparing nasopharyngeal swab and early morning saliva for the identification of SARS-CoV-2 [published online ahead of print August 6, 2020]. *Clin Infect Dis*. 2020:ciaa1156. https://doi.org/10.1093/cid/ciaa1156
12. Wyllie AL, Fournier J, Casanovas-Massana A, et al. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. *N Engl J Med*. 2020;383(13):1283-1286.
13. Goldfarb DM, Tilley P, Al-Rawahi GN, et al. Self-collected saline gargle samples as an alternative to healthcare worker-collected nasopharyngeal swabs for COVID-19 diagnosis in outpatients. *J Clin Microbiol*. 2021;59:e02427-20.

How to cite this article: Labbé A-C, Benoit P, Gobeille Paré S, et al. Comparison of saliva with oral and nasopharyngeal swabs for SARS-CoV-2 detection on various commercial and laboratory-developed assays. *J Med Virol*. 2021;93:5333-5338. https://doi.org/10.1002/jmv.27026