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► **To cite this version:**

Moustapha Dramé, Maturin Tabue Teguo, Emeline Proye, Fanny Hequet, Maxime Hentzien, et al.. Should RT-PCR be considered a gold standard in the diagnosis of Covid-19?. *Journal of Medical Virology*, 2020, 10.1002/jmv.25996 . hal-02883265

HAL Id: hal-02883265

<https://hal.science/hal-02883265>

Submitted on 15 Apr 2024

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Should RT-PCR be considered a gold standard in the diagnosis of COVID-19?

To the Editor,

To face the new coronavirus disease 2019 (COVID-19) pandemic, the need for early and accurate diagnosis of the disease among suspected cases quickly became obvious for effective management, and for better control of the spread of the disease in the population. Since the beginning of this disease epidemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), reverse transcriptase-polymerase chain reaction (RT-PCR) has routinely been used to confirm the diagnosis. However, several authors have pointed out the poor performance of this technique, particularly in terms of sensitivity.^{1,2} Indeed, according to some authors, sensitivity could be as low as 38%³ (ie, not better than chance). This made it necessary to find a more sensitive test, given the contagiousness of SARS-CoV-2. We, therefore, read with great interest the article published in your journal by Cassaniti et al.⁴ This article deals with the diagnosis of COVID-19 by serology (immunoglobulin m/immunoglobulin G) as a complementary approach to RT-PCR to improve its sensitivity. According to Cassaniti et al⁴ and Xiang et al,⁵ serology is faster to implement, less expensive, easier to use, and more accessible to staff with no specific laboratory training.⁵ The article describes the metrological performances of serology, and compare it with RT-PCR as the gold standard. Using a test as the gold standard when its metrological properties are clearly perfectible raises questions from a methodological point of view. Indeed, when an existing test is considered as a reference, this suggests that the test in question is always correct and that all misclassifications (false negatives and false positives) are due to the new test. However, the new test (in this case, serology) might be better than the old test (in this case, RT-PCR), but it would be impossible to demonstrate this. Consequently, the new test will never be able to achieve a sensitivity of 100%, since it is considered responsible for all misclassifications. The same mistake has also been made by other authors regarding the use of chest computed tomography scans as a diagnostic method.^{6,7} In this situation, the best strategy would be to measure the degree of agreement (using the Kappa coefficient measures⁸) between the two tests, that is, neither of the two tests is considered to be the reference and, therefore, any discrepancies could be linked to either of the tests. Thus, the serology performances presented by Xiang et al⁵ are certainly better than those presented in their paper.

The difficulty of using a gold standard is an old debate,^{9,10} but still relevant nonetheless. In the absence of an accurate reference

test, alternative strategies could be to perform the test repeatedly over time, to use the patient's clinical course, or the combination of several tests as the gold standard.


The purpose of writing this contribution is not to discuss the best diagnostic strategy for COVID-19, nor is it to question the results of the authors who used RT-PCR as a reference. On the contrary, it purports that their results might actually be even better than those presented.

ACKNOWLEDGMENT

The authors would like to thank Fiona Ecarnot, PhD, for editorial assistance.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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REFERENCES

1. Liu R, Han H, Liu F, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. *Clin Chim Acta*. 2020;505:172-175.
2. Xie J, Ding C, Li J, et al. Characteristics of patients with coronavirus disease (COVID-19) confirmed using an IgM-IgG antibody test [published online ahead of print April 24, 2020]. *J Med Virol*. 2020. <https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25930>
3. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients [published online ahead of print March 27, 2020]. *J Infect*. 2020;80(6): e14-e18.
4. Cassaniti I, Novazzi F, Giardina F, et al. Performance of VivaDiag COVID-19 IgM/IgG rapid test is inadequate for diagnosis of COVID-19 in acute patients referring to emergency room department [published online ahead of print March 30, 2020]. *J Med Virol*. 2020. <https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25800>
5. Xiang F., Wang X., He X., et al. Antibody detection and dynamic characteristics in patients with COVID-19 [published online ahead of print April 19, 2020]. *Clin Infect Dis*. 2020. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa461/5822173?searchresult=1>
6. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases [published online ahead of print February 26, 2020]. *Radiology*. 2020. https://pubs.rsna.org/doi/10.1148/radiol.2020200642?url_ver=Z39.88-2003&rft_id=ori%3Arid%3Acrossref.org&rft_dat=cr_pub++0pubmed&
7. Majidi H., Niksolat F. Chest CT in patients suspected of COVID-19 infection: a reliable alternative for RT-PCR. *Am J Emerg Med*. 2020.
8. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960;20:27-46.
9. Duggan PF. Time to abolish "gold standard". *BMJ*. 1992;304: 1568-1569.
10. Versi E. "Gold standard" is an appropriate term. *BMJ*. 1992; 305(6846):187.