

GEBRUIK VAN SNELLE RT-PCR TESTS VOOR DE OPSPORING VAN SARS-COV-2

RAG subgroep Testing – 19 april 2021

Opmerking: De huidige aanbevelingen zijn onderhevig aan veranderingen afhankelijk van nieuwe wetenschappelijke gegevens en/of de evolutie van de epidemie.

Samenvatting en aanbevelingen:

- Snelle reverse transcriptase PCR tests (RT-PCR) die een resultaat geven in minder dan een uur, zoals GeneXpert, hebben een gelijkaardige betrouwbaarheid als de standaard RT-PCR tests en zijn daarom een valabel alternatief.
- Wegens hun hogere kost en hun lagere verwerkingscapaciteit zijn ze enkel aangewezen in situaties waar snel een resultaat vereist is.
- Wegens hun beperkte beschikbaarheid worden ze best voorbehouden voor indicaties waar ze het meest nodig zijn.
- We bevelen daarom aan om ze enkel in een hospitaal setting te gebruiken in de volgende situaties:
 - diagnose bij patiënten met ernstige symptomen van COVID-19 die dringend in het ziekenhuis moeten worden opgenomen;
 - screening op SARS-CoV-2 bij niet-COVID patiënten die een dringende medische ingreep vereisen;
 - screening op SARS-CoV-2 bij niet-COVID gehospitaliseerde patiënten waarbij effectieve preventieve maatregelen niet of moeilijk haalbaar zijn (bijvoorbeeld: patiënten die een kamer delen, bevallende moeders).
- Gebruik buiten een hospitaal setting wordt momenteel afgeraden.
- Het te gebruiken staal is datgene dat door de fabrikant wordt aanbevolen. In de meeste gevallen zal dit een nasofaryngeale wisser zijn.

De volgende personen hebben deelgenomen aan dit advies:

Emmanuel André (KU Leuven); Bénédicte Delaere (UCLouvain); Olivier Denis (CHU-UCL Namur); Herman Goossens (UAntwerpen); Marie Pierre Hayette (CHU-Liège); Yves Lafort (Sciensano); Barbara Legiest (ZG); Tinne Lernout (Sciensano); Pieter Libin (UHasselt); Romain Mahieu (COCOM); Elizaveta Padalko (UZGent); Olivier Vandenberg (LHUB-ULB); Ann Van den Bruel (KU Leuven); Steven Van Gucht (Sciensano); Pieter Vermeersch (KU Leuven).

CONTEXT

Rapid and accurate (with PCR) differential diagnosis between infected persons and non-infected persons is crucial in curbing outbreaks in structural collectivities, in particular in hospitals. In the latter, the outbreak management starts in the emergency departments and the deployment of rapid PCR testing is an important cornerstone in this process. However, such faster SARS-CoV-2-PCR tests with a turnaround time of less than 60 minutes have a significantly higher cost. In addition, in some hospitals it may be interesting to place these systems close to the emergency departments (PoC) which additionally results in an extra training cost. The current nomenclature foresees a reimbursement based on the cost of a regular RT-PCR. The RAG Testing was requested to provide an advice on the usefulness and the potential indications of this type of tests.

DISCUSSION

- A difference need to be made between rapid Nucleic Acid Amplification Tests (NAATs), using reverse transcriptase polymerase chain reaction (RT-PCR), such as GeneXpert, and rapid NAATs using other methods, such as isothermal amplification (LAMP, TMA, SDA). The latter are less sensitive than the first that have a similar performance to the standard RT-PCR tests. The current recommendations only apply to rapid tests using RT-PCR.
- Availability of rapid RT-PCR tests is limited and they should therefore be reserved for situations where they really have an added value. The use of these tests for screening purposes (as for example currently in the Ecolog testing center at Brussels airport) should be discouraged, or even prohibited.
- Rapid RT-PCR tests are more expensive than the standard RT-PCR tests. In addition their overall throughput is 4-5 times lower than RT-PCR tests. Therefore, if the result is not needed rapidly, a standard RT-PCR is the preferential choice.
- Urgent results are mostly needed in a context of severe disease or in a context of screening before an urgent medical intervention (for example transplantation), or in a context where strict respect of protective measures is difficult, such as hospitalization of two patients in the same (double) room or childbirth. Rapid RT-PCR tests are therefore most useful at hospitals and hospital emergency departments.

RECOMMENDATIONS

- Rapid RT-PCR tests have a similar performance to standard RT-PCR tests and are therefore a valid alternative.
- Their use should be reserved for situations where an urgent and accurate result is needed. We therefore recommend to only use them in hospital settings for:
 - diagnosis in patients with severe symptoms of COVID-19 who require urgent hospitalization;
 - screening for SARS-CoV-2 in patients who require an urgent medical intervention;

- screening for SARS-CoV-2 in hospitalized patients where effective preventive measures are not feasible or difficult to implement (for example: patients who share a same room, mothers giving birth).
- The availability of rapid RT-PCR tests is limited. We therefore do not recommend to use them in any other setting, such as for routine screening in asymptomatic patients outside a hospital setting.
- The preferred sample to use is that recommended by the manufacturer's instructions. In most cases this will be a naso-pharyngeal swab.

BACKGROUND

Rapid molecular tests for detecting SARS-CoV-2

Nucleic Acid Amplification Tests (NAATs) are the standard tests for the detection of SARS-CoV-2. Most commonly this is through reverse transcriptase polymerase chain reaction (RT-PCR) and most RT-PCR tests take 4 to 6 hours to get the result. However, certain NAATs provide faster results (in about 15–45 minutes), and these are often referred to as 'rapid PCR tests'. These tests use different techniques. Some use RT-PCR (such as GeneXpert), others isothermal amplification methods, such as transcription mediated amplification (TMA), strand displacement amplification (SDA) or loop-mediated isothermal amplification (LAMP), and others use CRISPR-Cas technology (1,2).

Some rapid PCR tests are laboratory-based, others can be used at the point-of-care (PoC) (3). Platforms for PoC PCR tests can be mobile (small and portable) or facility-based. Mobile platforms process fewer samples in a specified timeframe and typically run one sample at a time in 5-30 minutes. Facility-based platforms (such as for example GeneXpert Xpress) have higher throughput than the mobile platforms, but still return results in less than an hour. The components are often self-contained, requiring fewer laboratory resources (i.e., hands-on personnel) than other laboratory-based instruments.

The FDA has approved two rapid PCR Tests for self-testing in home and community settings: the Cue COVID-19 Test for Home and Over The Counter (OTC) Use (Cue Health Inc.) and the Lucira COVID-19 All-In-One Test Kit (Lucira Health, Inc.). No such tests have been approved for the European market yet.

Performance compared to the standard RT-PCR

Numerous studies have evaluated the performance of different rapid PCR tests.

A review of the evidence by the Infectious Disease Society of America identified 19 studies that assessed diagnostic test accuracy of rapid RT-PCR or rapid isothermal NAAT versus standard methods in symptomatic patients (4). Rapid RT-PCR tests had a pooled sensitivity of 97% (95% CI: 94-99) and a specificity of 96% (95% CI: 94-98). In a subgroup of studies that allowed direct comparison of the diagnostic accuracy of rapid RT-PCR and standard laboratory-based NAAT using a composite reference standard, the sensitivity and specificity of **rapid RT-PCR** were comparable to standard laboratory-based tests (98% [95% CI: 95-100] vs. 98% [95% CI: 95-99] and 97% [95% CI: 89-99] vs. 97% [95% CI: 92-99], respectively. **Rapid isothermal NAAT** had a sensitivity of 70% (95% CI: 56-81) and a specificity of 99% (95% CI, 97-99), and in the above mentioned subgroup, a lower sensitivity than standard laboratory-based tests

(81% [95% CI: 75-86] vs. 99% [95% CI: 97-100]) but comparable specificity (99% [95% CI: 96-100] vs 97% [95% CI: 93-99]).

A recent Cochrane review of 30 studies evaluating five different rapid molecular tests, found an average sensitivity of the ID NOW assay (an assay of Abbott using isothermal NAAT) of 73.0% (95% CI 66.8-78.4) and an average specificity of 99.7% (95% CI 98.7-99.9), and an average sensitivity of 100% (95% CI 88.1-100) and an average specificity of 97.2% (95% CI 89.4% to 99.3%) of the Xpert Xpress assay (a GeneXpert assay of Cepheid using RT-PCR). The authors concluded that a small number of molecular tests showed high accuracy and may be suitable alternatives to RT-PCR. However, further evaluations of the tests in settings as they are intended to be used are required to fully establish performance in practice.

International guidelines

No guidance on the use of rapid PCR tests was identified from international agencies, such as the WHO or ECDC. Also, only few countries have issued guidelines on the use of rapid PCR tests.

USA

The Infectious Disease Society of America recommends using either rapid RT-PCR or standard laboratory-based NAATs over rapid isothermal NAATs (4). They consider rapid isothermal NAATs, however, as an acceptable testing option when rapid RT-PCR or standard laboratory-based NAAT is not readily available. A negative rapid isothermal test result from an individual with a high clinical suspicion for SARS-CoV-2 infection, or anyone in a moderate (10%) or high prevalence (40%) population, should be confirmed by standard NAAT or a rapid RT-PCR test when testing is available and the results will affect patient management.

CDC states that the sensitivity of laboratory-based NAATs is generally high and moderate-high for POC NAATs (5).

The Netherlands

The RIVM of the Netherlands only gives advice on the use of the LAMP test. It states that it has a similar accuracy as the standard RT-PCR test and that it can be used when the results are needed faster (6).

Current uses in Belgium

In certain hospitals a rapid PCR test is used when a rapid result is required, such as in severely ill people.

At Brussels airport, Ecolog operates a testing center that offers testing to both departing and arriving (asymptomatic) passengers. The tests offered are either a standard PCR test (€67) or a rapid PCR test (€135) (7).

Current recommendations in Belgium

In the [testing strategy update of August 2020](#), recommendations were given on the use of the RT-LAMP test. It was recommended not to use RT-LAMP as a diagnostic tool for symptomatic individuals or contacts nor for screening of an asymptomatic population because of the lack of wide scale validation studies, at that time. However, since results of non-commercial assays were promising, developments in the area were to be followed closely.

REFERENCES

1. Abduljalil JM. Laboratory diagnosis of SARS-CoV-2: available approaches and limitations. *New Microbes New Infect.* 2020 Jul;36:100713.
2. Yan Y, Chang L, Wang L. Laboratory testing of SARS-CoV, MERS-CoV, and SARS-CoV-2 (2019-nCoV): Current status, challenges, and countermeasures. *Rev Med Virol.* 2020 May;30(3):e2106.
3. OASH-COVID-19-guidance-testing-platforms.pdf [Internet]. [cited 2021 Apr 7]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/downloads/OASH-COVID-19-guidance-testing-platforms.pdf>
4. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19 [Internet]. [cited 2021 Apr 7]. Available from: <https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/>
5. CDC. Healthcare Workers [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2021 Apr 7]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>
6. De PCR-test | RIVM [Internet]. [cited 2021 Apr 7]. Available from: <https://www.rivm.nl/coronavirus-covid-19/testen/pcr-test>
7. Covid-19 Test Centre [Internet]. Brussels Airport Website. [cited 2021 Apr 7]. Available from: <https://www.brusselsairport.be/en/passengers/the-impact-of-the-coronavirus/covid-19-test-centre-at-brussels-airport>