

Fast-track ruling in/out SARS-CoV-2 infection with rapid 0/1.5 h molecular test in patients with acute coronary syndromes

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Aims Patients with acute coronary syndrome (ACS) often arrive in the catheterization (cath) lab directly from the field or an emergency department without an accurate triage for Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Although in the pandemic period the treatment in the cath laboratory of high-risk ACS should not be delayed because the operators wear special protection systems, the subsequent risk of contagion in a non-Covid coronary care unit could be high in the case of patients positive for SARS-CoV-2.

Methods We tested the possibility of a fast-track protocol in 51 consecutive patients (mean age 65 ± 12 years) transferred from spokes centres or from the field to our HUB centre and admitted to our coronary care unit (CCU). Once the patient had arrived in the cath lab, the nasopharyngeal swab was performed. The real-time PCR to extract RNA for SARS-CoV-2 detection was performed with an automated rapid molecular Xpert Xpress test. Meanwhile, coronary angiography or percutaneous coronary intervention was performed if necessary.

Results In this fast-track protocol, the time to perform nasopharyngeal swab was 11 ± 11 min; time spent to transport nasopharyngeal swab to the laboratory was 29 ± 20 min; time to detect viral nucleic acid was

68 ± 16 min. The overall time from the execution of nasopharyngeal swab to the result was 109 ± 26 min. The results were immediately put into the hospital computer system and made readily available. Depending on the test result, patients were then transferred to the regular CCU or Covid area.

Conclusion This study demonstrates that 0–1.5 h fast-track triage for coronavirus disease 2019 (COVID 19) is feasible in patients with ACS. The execution of nasopharyngeal swab in the cath lab and its analysis with a rapid molecular test allows rapid stratification of SARS-CoV-2 infection.

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Introduction

Patients with acute coronary syndromes (ACS) often arrive in the catheterization (cath) laboratory directly from the territory or from an emergency department without an accurate triage for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Although in the pandemic period the treatment in the cath lab should not be delayed because the operators wear special protection systems, the subsequent risk of contagion in a non-COVID coronary care unit (CCU) could be high in the case of patients positive for SARS-CoV-2.^{1–3}

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Several documents/protocols from scientific societies with a series of recommendations for cardiac catheterization laboratory procedures during the coronavirus disease-19 (COVID-19) pandemic are currently available.^{4,5} Hospitals are encouraged to develop local protocols in order to properly triage, diagnose and treat patients with ACS during the COVID-19 pandemic, without unnecessarily exposing healthcare personnel and other patients to a possible contagion. However, for selected acute patients, a proper triage is not always possible. In addition, several individuals could be SARS-CoV-2 positive without symptoms. Therefore, SARS-CoV-2 screening tests that would permit the well tolerated admission into a non-COVID division after percutaneous coronary procedures should be implemented. Because the immediate

Table 1 Baseline clinical features of the study population

	Rapid test (n = 51)
Age (years) \pm SD	65 \pm 12
Male, n (%)	40 (78)
Hypertension, n (%)	40 (78)
Diabetes, n (%)	11 (22)
Dyslipidaemia, n (%)	39 (76)
Smokers, n (%)	8 (16)
Prior MI, n (%)	8 (16)
Prior stroke/TIA, n (%)	1 (2)
Obesity, n (%)	6 (12)
COPD, n (%)	3 (6)
Fever, n (%)	1 (2)
Pneumonia, n (%)	0 (0)

ACS, acute coronary syndrome; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; TIA, transient ischemic attack.

serologic tests are nonrecommended, molecular SARS-CoV-2 testing real-time PCR should be obtained as quickly as possible in acute patients admitted to the hospitals for coronary angiography and percutaneous coronary intervention (PCI). To date, there are many new rapid molecular diagnostic FDA/CE-approved tests that could be used in these acute patients.

Accordingly, this study aimed to evaluate the feasibility of a fast-track protocol to rule in/out SARS-CoV-2 infection in acute coronary syndrome patients.

Materials and methods

Fifty-one patients urgently admitted to our institution were included in this feasibility study. The Ethical Committee of the University Magna Graecia approved the study and all individuals gave written informed consent. The characteristics of patients are reported in Table 1.

Fast-track molecular testing

The patients were transferred from spokes centres and from the territory to our HUB centre through a dedicated pathway. As soon as the patient had arrived in the cath lab, the interventional cardiologist, before the coronary angiography and with adequate COVID 19 protection systems,^{4,5} performed a nasopharyngeal swab. The biological materials were collected by nasopharyngeal swab specimens.⁶

At the end of the coronary invasive procedure, the test result was considered mandatory to transfer the patient to the non-COVID CCU or Covid ICU.

In consideration of the need to know the result of the SARS-CoV-2 virus test as quickly as possible, patients were tested using the Xpert Xpress SARS-CoV-2 system (Cepheid, Sunnyvale, USA) that received authorization to be used in an emergency regime by the United States Food and Drug Administration on 20 March 2020. GeneXpert platforms were already available in our institution and currently used for the diagnosis of tuberculosis (TB) and resistance to rifampicin (as recommended by the

WHO), hepatitis C, seasonal flu, HIV viral load and for the early diagnosis of HIV infection.

Xpert Xpress SARS-CoV-2 is an in-vitro diagnostic test that uses real-time PCR on disposable cartridges in which there are all ready-to-use reagents to perform the phases of extraction, amplification and detection of viral nucleic acid, targeting the viral genomic regions N2 and E. The cartridge was loaded with 300 μ l of a biological patient's sample taken by the nasopharyngeal swab. Subsequently, it was positioned into the GeneXpert instrument wherein the test was performed automatically in about 45 min. The Xpert test provided sensitive and accurate detection of SARS-CoV-2 in a variety of upper and lower-respiratory-tract specimens.^{7,8}

The positive agreement of the Xpert test was tested using 483 upper and lower-respiratory-tract specimens previously analysed by standard-of-care (SOC) NAATs.⁷ The positive agreement of the Xpert test was 219/220 (99.5%) and the negative agreement was 250/261 (95.8%).⁷

The timing needed to perform the nasopharyngeal swabs, transport them to the laboratory and obtain real-time PCR with the rapid test was calculated.

Results

Fast-track molecular testing

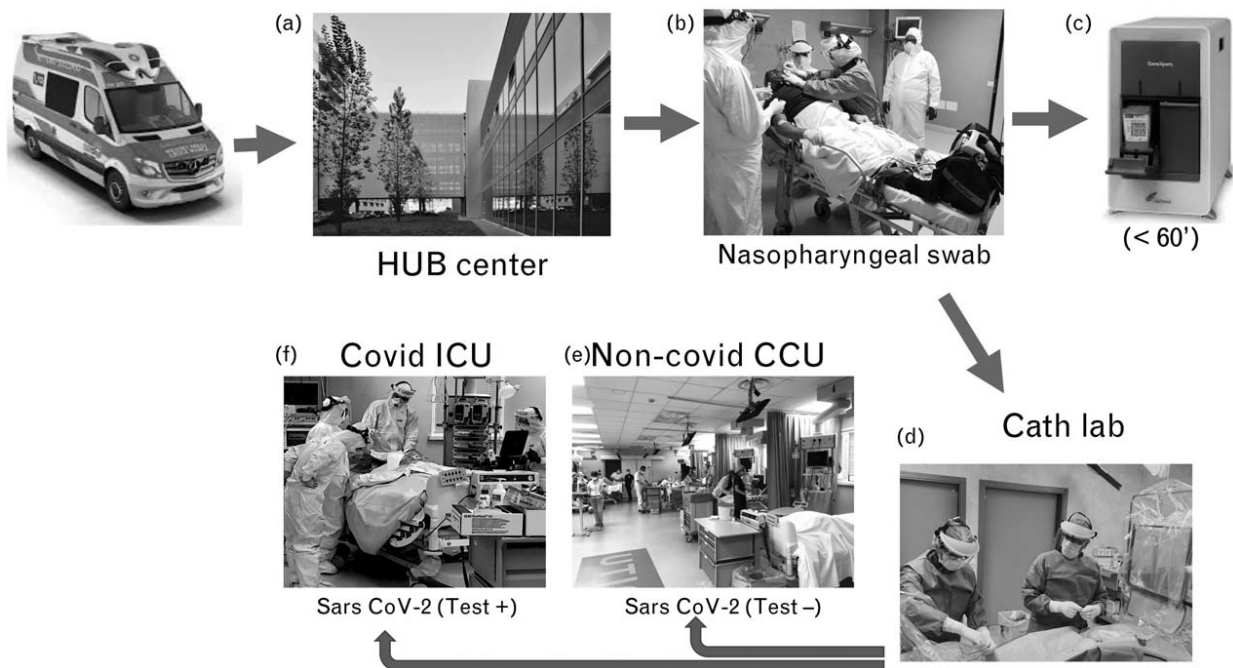
From 25 April to 10 June 2020, 51 patients of mean age 65 + 12 years, of whom 40 men (78%) were transferred from the emergency system to the Cardiology Division of the Magna Graecia University of Catanzaro were included in the study.

After admission to the CCU, the diagnosis was in 24 patients (47%) STEMI, 12 patients (24%) NSTEMI, 9 patients (18%) unstable angina and in 6 patients (12%) acute heart failure.

The clinical features of the patients are reported in Table 1. All but one patient tested with a nasopharyngeal swab for molecular SARS-CoV-2 research were negative. Figure 1 shows the protocol used in our institution during the SARS-CoV2 pandemic. During the pandemic, every new patient with ACS was considered potentially infected by COVID-19 and, after the procedures, isolated in dedicated rooms until the test was available.

Patients with ACS were transferred through the emergency system to our cath lab centre using a dedicated path and elevators. In the cath lab, the nasopharyngeal swab specimens were performed by the interventional cardiologist.⁶ Then, the coronary angiography and PCI were performed, if necessary, by the adequately protected staff. At the end of the invasive procedure, on the basis of the results of the molecular test, the patients were transferred to the COVID ICU or non-COVID CCU rooms.

Fig. 1



The figure shows the protocol used in the study at Magna Graecia University. In (a): dedicated path for patients with suspicion of COVID-19. In (b): execution nasopharyngeal swab in the cath lab. The swab is processed with the rapid Cepheid system (c) and the coronary angiography was started (d). According on swab results, patients were transferred to the non-COVID CCU (e) or COVID ICU (f).

Because the primary objective was to identify any possible patients positive for SARS-CoV-2 infection as soon as possible and obviously before the patient was transferred to the non-COVID CCU, the times of several steps were calculated. The time to perform nasopharyngeal swab in the cath lab was 10 ± 10 min. The time spent to transport the nasopharyngeal test to the analysis laboratory was 30 ± 20 min. The time to load $300 \mu\text{l}$ of biological material and the extraction, amplification and detection of viral nucleic acid, targeting the viral genomic regions N2 and E was 68 ± 15 min. The overall time from the execution of nasopharyngeal swab to the result was 109 ± 26 min. The results were immediately put into the hospital computer system and made readily available.

Discussion

The major finding of this study was the feasibility of a fast-track path with a rapid molecular SARS-CoV-2 test to quickly rule in/out the diagnosis of COVID-19.

On 30 January 2020, the WHO declared coronavirus disease 2019 (COVID-19) to be a public health emergency of international concern, and on 11 March 2020, a global pandemic that affected 21.2 million confirmed COVID-19 cases including 761 000 deaths in 216 countries (<https://www.who.int>). Many developed countries, including Italy, were simply unprepared and the

nasopharyngeal tests were not available in the hot phase of the pandemic for ACS patients.⁹

Therefore, the needing for rapid and accurate laboratory molecular tests for the detection of the SARS-CoV-2 virus has been highlighted especially in the setting of ACS. The organization of dedicated pathways could include the possibility to perform a rapid molecular test for COVID-19.

Patients with ACS need rapid hospitalization, which often does not allow adequate triage procedures. Patients diagnosed with high-risk ACS are quickly transferred to the cath lab for coronary angiography and PCI if needed. Therefore, it is mandatory to have a molecular test result available as soon as possible, ideally at the end of the procedures. Preferably, all patients with ACS should be rapidly tested to rule out the possibility of being affected by SARS-Cov2 and, after PCI, must be transferred to the regular CCU only if the COVID-19 test is negative.

In the COVID-19 period, the number of hospitalized patients for myocardial infarction was significantly reduced mainly for the contagion fear.⁹ In addition, in patients presenting with STEMI and concurrent COVID-19 infection, there is a strong signal towards higher thrombus burden and poorer outcomes.¹⁰ In

COVID-19, inflammation induced by the infection might be a trigger for ACS.¹¹

The possibility to perform rapid tests during the pandemic could be useful in the triage of patients with ACS in the pandemic period as an option to reduce the in-hospital dissemination of the infection.

In our study, we used the Xpert Xpress system, a recent FDA-approved test,⁸ that does not need a phase of laboratory preparation of the sample to be analysed. The rapid test performs real-time PCR on disposable cartridges with ready-to-use reagents to carry out the extraction, amplification, and detection of the nucleic acid and the possibility to analyse a single sample at a time. This system avoids the problem of collecting a minimum of 24 samples of the classic method. A recent study comparing FDA emergency use authorized assays for SARS-CoV-2 (Cepheid, DiaSorin, Hologic Panther and Roche Cobas) demonstrated that the Cepheid Xpert Xpress SARS-CoV-2 assay was a sensitive assay for SARS-CoV-2 with 100% agreement and specificity across specimens.¹² Recently, the Cepheid Xpert Xpress SARS-CoV-2 demonstrated comparable performance also with Roche Cobas SARS-CoV-2.¹³ Another European study evaluated the Xpert Xpress SARS-CoV-2 against the routine in-house real-time RT-PCR assays in three medical microbiology laboratories in the Netherlands.¹⁴ In this study, the Xpert Xpress SARS-CoV-2 point-of-care test showed equal performance compared with routine in-house testing with a limit of detection (LOD) of 8.26 copies/ml. In clinical samples, Xpert Xpress SARS-CoV-2 reaches an agreement of 100% compared with all in-house RT-PCRs and the assay outperforms routinely used diagnostic platforms in the sensitivity panel.¹⁴

Possible advantages of the Xpert Xpress system are that the assay is fully automated and provides results theoretically within 45 min. However, laboratory staff may be already familiar with the GeneXpert platform, given that the Xpert MTB/RIF assay serves as the primary diagnostic assay for TB, as suggested by the WHO.¹⁵ As the WHO pointed out, Xpert Xpress SARS-CoV-2 is a promising option for testing a limited number of samples (e.g. from patients in ICUs or healthcare workers with the highest public health priority). It is probably not the optimal solution for a large scale of samples.¹⁵

There are several rapid tests available that could be used in the catheterization laboratories and in the intensive care units.

Serological or rapid antigen tests are available but currently not recommended by the WHO for COVID-19 case detection. Nucleic acid amplification tests remain the standard for the diagnosis of SARS-CoV-2 infection.

The new 'Id-Now COVID-19' portable molecular test that is capable of delivering positive results in just 5 min and negative results in 13 min was recently approved by

the FDA. The test has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens, and is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in-vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.¹⁶ The sensitivity of Id-Now COVID-19 was 71.7% and all false-negative results correlated to those samples that were weakly positive¹⁷ (that could be frequently observed in patients in phase 2 of the COVID-19 pandemic). A recent study demonstrated that the Id-Now COVID-19 had negative results in one-third of the samples that tested positive by Cepheid Xpert Xpress when using nasopharyngeal swabs in viral transport media.¹⁸

In our institution, we started this new study protocol in patients with ACS using the Xpress Xpert method to quickly rule in or rule out the SARS-CoV-2 infection. Using this protocol, the nasopharyngeal swab was performed before starting the procedures in the cath lab. At the end of the interventional procedure, on the basis of the test results, the patients were transferred to normal CCU only if COVID-19 negative (Fig. 1). This method was very useful because when previously using a standard technique the response in our institution was available in about 600 min. In contrast, the overall time from the execution of the nasopharyngeal swab to the result using the Cepheid Xpert Xpress test was 109 ± 27 min. However, this time could be further reduced decreasing by the optimization of all processes (i.e. transport of the swabs and further reducing the delay in the virology laboratory). Therefore, applying this new protocol, it is possible to avoid a delayed diagnosis of SARS-CoV-2 that could have serious consequences for other patients admitted to the ICU or CCU and for medical and health personnel.

Of course, the potential benefit of ruling out SARS-CoV-2 infection with a rapid 0/1.5 h molecular test could be useful also in acute patients who have undergone percutaneous aortic implantation (Transcatheter aortic valve implantation),^{19,20} as well as the percutaneous repair of the mitral valve.²¹

Limitations of the study

The implementation of this protocol needs the GeneXpert platforms that in our institution were already available and currently used for the diagnosis of TB and resistance to rifampicin, hepatitis C, seasonal flu, HIV viral load, and for the early diagnosis of HIV infection. Although the laboratory Xpress Xpert method for quick testing for SARS-CoV-2 is simple, trained technical personnel are required. Finally, the cost/benefit implications of universally testing all such patients need to be further studied.

Conclusion

This feasibility study demonstrates that 0–1.5 h fast-track triage for COVID-19 is possible in patients with ACSs. The execution of nasopharyngeal swab in the cath lab and its analysis with a rapid molecular test allows rapid stratification of SARS-CoV-2 infection.

Conflicts of interest

There are no conflicts of interest.

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