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Is Computed Tomography Necessary for the Diagnosis of Coronavirus Disease (COVID–19) in all Suspected Patients? a case series

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Abstract

Coronavirus disease 2019 (COVID–19), reported pandemic in March 2020, is the current health problem with no definite prevention or treatment. As a newly emerging disease, new cases are reported each day to add to the physician's knowledge about the best clinical approach. One of the controversies in this regard is the gold standard diagnostic method. Evidence suggests that polymerase chain reaction (RT–PCR) for Coronavirus nucleic acid has a low sensitivity and computed tomography (CT) has been suggested for more accurate diagnosis. Yet, CT has the disadvantage of radiation and is not safe in all patients. Here, we present a case series of 23 patients who underwent both RT–PCR and CT and report the outcome.

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Introduction

Coronavirus disease 2019 (COVID–19), also known as 2019 novel Coronavirus (2019–n CoV), is today a critical health issue, affecting more patients each day with a worldwide mortality exceeding 300,000 patients until 05/20/2020 (1). It emerged from Wuhan, China in December 2019, and spread rapidly throughout the world by human–to–human transmission, with an R0 of 2.5-3.5 (2, 3), resulting in the worst influential pandemic in new era, without any preventive or definite treatment measure, to date (4). Although the main infection site is the respiratory system, which results in cough, breathlessness, and pneumonia, many patients may present with nonspecific symptoms, such as fever, headache, fatigue, malaise, and sore throat (5) and some may also be completely asymptomatic (carriers), which makes diagnosis difficult (6). As the main step for reducing the disease spread is early diagnosis of the infected individuals and their isolation. The

first and utmost important issue in COVID–19 is definite diagnosis, which is the focus of the current research.

Some have suggested taking history of close contact or exposure to infection for diagnosis of COVID–19 (5); however, by the lasting existence and wide and rapid growth of the virus throughout the world, many may be unaware of their exposure. The most commonly used diagnostic method is real time reverse transcriptase polymerase chain reaction (r-RT-PCR) (7). However, there are several issues affecting the results of RT–PCR, such as the kit's accuracy, the quality of the collected sample, and the test performance (8), which make high rate of false–negative and some false–positive results; these factors suggest that the results of RT–PCR should be interpreted with great caution; notably, a negative RT–PCR result should not be used to rule out COVID–19 (9). Thus, studies have suggested performing high resolution computed tomography (HRCT) scan of the chest with a sensitivity of 98% for definite diagnosis of the disease (10), which shows hallmarks of the lung involvement by COVID–19, even in patients with negative RT–PCR results (11, 12). But since chest HRCT has the risk of radiation exposure and is contraindicated for some patients, it is not safe to be used for everyone as a screening test (13). Nevertheless, guidelines suggest testing asymptomatic patients by laboratory tests (14). The issue remaining is the best diagnostic method to be used in all patients. Due to the importance of knowing which patients should undergo chest HRCT, and which RT–PCR alone, for definite diagnosis of COVID–19, here, we present a series of 23 patients with clinical, RT–PCR, and HRCT results of COVID–19 in order to compare the results of these two tests, compared to the final diagnosis, discuss the clinical outcome of these patients, and estimate the false negative and false positive rates of these tests, namely RT–PCR and HRCT.

Materials and Methods

All patients who were supposed to be admitted to Pars hospital, Tehran, Iran, during April 2020, for the treatment of their underlying disease or limb injury due to car accident were included. RT–PCR and HRCT were performed for all patients. For RT–PCR for COVID–19 nucleic acid, sampling from nasopharyngeal and oropharyngeal swabs (Dacron or Rayon swabs) were taken by a trained personnel, while considering the biosafety instructions. The samples were immediately transported to the hospital's laboratory in the same tube with viral transport medium. At the laboratory, the viral nucleic acid was extracted from the swabs using Magpurix 24 automated Nucleic Acid purification system (Zinext life science corp, Resnova, Rome, Italy), Mage core extraction system (RBC bioscience, Taipei), and the commercially available viral nucleic acid extraction kit. RT–PCR was performed for the detection of SARS–COV–2 on Biorad CFX–96 RT–PCR machine (made in USA) and Sansure Biotech In., China. For this purpose, novel Coronavirus (2019–nCov) nucleic acid diagnostic kit (PCR–Fluorescence probing) was used for molecular detection of the opening reading frame 1 lab and the specific conserved sequence of coding protein nucleocapsid from suspected cases. Detection of typical S–shape amplification curve at fluorescein amidites and/or 6–carboxy Rhodamine channel, and the internal control amplification curve, detected at cyanin–5 channel, cycle threshold ≤40 indication of positive result.

The HRCT images were taken using Siemens Scope power sensation 16 Slice machine (2017) and separately interpreted by two radiologists, who were blind to the results of PCR of each patient. The typical and atypical CT findings suggested by Salehi et al. were used for the diagnosis of COVID–19 (15).

Results

The test results of RT–PCR were positive in 10/23 patients and that of chest HRCT was positive in 18/23 patients. Demographic information were collected from patients, including patients' age and sex, smoking, history of underlying diseases, allergy, sinusitis, H_1N_1, and number of common colds in the last year (Table 1). The mean age of the studied patients was 53.82 years and 56.5% were female. Five patients were smokers. Eight patients had no underlying disease and the rest had a variety of diseases including diabetes mellitus (n=6), hypertension (n=7), cardiovascular disease (n=4), cancer (n=3), history of allergy (n=5), sinusitis (n=3) and only one patient reported positive history of H_1N_1.

Table 1. The demographic characteristics and past medical history of the studied patients

Case No.	Age (year)	Sex	Smoking	PMH	Allergy	Sinusitis	H1N1 or cc	No of common colds
1	72	Male	+	DM, HTN	-	-	-	1
2	65	Female	-	DM, CVD, HTN	-	-	-	0
3	48	Male	+	Cancer	+	-	-	2
4	64	Female	-	HTN, PD	+	-	-	1
5	61	Male	+	PD	+	-	-	0
6	60	Male	-	others	-	+	-	0
7	65	Female	-	DM, others	-	-	+	1
8	67	Male	+	HTN	+	-	-	0
9	62	Female	-	HTN	-	-	-	0
10	72	Male	+	DM, CVD, PD	-	-	-	1
11	36	Male	-	0	+	+	-	0
12	66	Female	-	Cancer, HTN	-	+	-	1
13	65	Female	-	CVD	-	-	-	0
14	55	Female	-	DM, cancer	-	-	-	0
15	36	Male	-	0	-	-	-	0
16	25	Female	-	0	-	-	-	0
17	78	Female	-	DM	-	-	-	1
18	39	Female	-	0	-	-	-	0
19	41	Male	-	0	-	-	-	0
20	41	Female	-	0	-	-	-	0
21	79	Female	-	CVD, HTN	-	-	-	1
22	31	Female	-	0	-	-	-	0
23	10	Male	-	0	-	-	-	0

Abbreviations: DM: diabetes mellitus, HTN: hypertension, CVD: cardiovascular disease, PD: pulmonary disease

The following information was also collected, including exposure to COVID–19, symptoms of COVID–19, incubation period, and duration of hospitalization and treatment for COVID–19, the results of which are reported in table 2. Ten patients had no exposure to COVID–19. The most common symptom was fever (observed in 8 patients), followed by muscle pain and fatigue (observed in 6 patients), breathlessness (observed in 4 patients), and cough (observed in 3 patients) and 7/23 had no symptoms. The mean incubation period was 2.69 days (excluding the three without COVID–19). Two were admitted at ICU, 6 at ward, and the rest were not hospitalized. Mean duration of hospitalization was 8.22 days. Of all patients, three received no treatment and, substantially, COVID–19 was ruled out in those patients; the rest were hospitalized and received treatment with a mean duration of 8.4 days. After treatment, RT–PCR and HRCT were repeated. The results of the 2nd RT–PCR was positive in 4/23 and negative in 9/23 (10 patients refused to redo the test) and that of HRCT was positive in 7/23 and negative in 9/23 (7 patients refused to redo the test).

Table 2. The COVID–19 characteristics of the studied patients

	Exposure	Symptoms	Incub. Period (days)	Duration of disease (days)	Admission period (days)	ICU admission	1st PCR	2nd PCR	1st CT	2nd CT	Duration of treatment
1	-	MPF	3	15	15	-	+	NA	-	NA	15
2	+	-	2	10	3	-	+	NA	-	NA	5
3	+	No smell	2	7	0	NA	+	NA	-	NA	7
4	+	fever, B	1	14	3	NA	+	NA	-	NA	5
5	+	Nasal congestion	1	7	7	-	+	-	+	-	5
6	-	-	0	0	0	NA	+	NA	-	NA	0
7	-	-	0	0	0	NA	+	-	+	-	0
8	+	-	0	21	0	NA	+	-	+	+	5
9	-	-	0	28	0	NA	+	-	+	NA	12
10	+	B	1	7	6	+	+	-	+	-	5
11	-	fever, MPF	2	12	0	NA	-	NA	+	NA	12
12	-	fever, MPF	2	14	14	-	-	-	+	-	14
13	+	B	3	14	0	NA	-	NA	+	+	14
14	-	cough, B	3	10	0	NA	-	+	+	+	10
15	-	fever, MPF	1	10	0	NA	-	+	+	+	5
16	-	-	0	3	0	NA	-	-	+	-	0
17	-	Fever	3	14	10	-	-	+	+	+	14
18	+	-	0	3	0	NA	-	NA	+	-	5
19	+	cough, MPF	5	10	0	NA	-	NA	+	+	10
20	+	Cough, MPF	6	10	0	NA	-	NA	+	+	10
21	-	fever	3	7	6	+	-	-	+	-	5
22	-	fever, cough, no smell	3	14	0	NA	-	+	+	-	5
23	-	fever, GI problem	3	10	10	-	-	-	+	-	5

Abbreviations: MPF: muscle pain, and fatigue, GI: gastrointestinal, B: breathlessness, Incub.: incubation, ICU: intensive care unit

Discussion and conclusion

In this case series, we presented the clinical characteristics, diagnosis, and treatment procedure of patients, admitted to our hospital, which revealed interesting results. One of the important notices is about the presenting clinical symptoms, as 7 had no symptoms at admission, among whom COVID–19 was confirmed in 4, three were treated for 5 days and one for 12 days. This finding emphasizes that the clinical symptoms of COVID–19 are not reliable for the diagnosis and asymptomatic cases may also have COVID–19 (16), which is very important from the epidemiologic point of view, as asymptomatic patients may transmit the disease (17). This issue has raised the importance of early and definite diagnosis of COVID–19 by paraclinical tests, which include RT–PCR, serum antibodies, and chest HRCT; considering that antibody tests will not be positive until the final disease course (18).

In our study, we examined all patients with RT–PCR and HRCT and evaluated the response to treatment by repetition of these tests. The results showed that RT–PCR was only positive in less than half of the patients, while the majority had positive results of chest HRCT. This finding has two aspects; first, it confirms the notice that the results of RT–PCR for COVID–19 nucleic acid should be interpreted with great caution and a negative RT–PCR should not be considered for ruling out COVID–19 (19). As indicated previously (10), chest HRCT has a higher sensitivity, compared to RT–PCR (98% vs. 71%, respectively); therefore, chest HRCT has been suggested for the diagnosis, management, and follow–up of patients with COVID–19 (20, 21), especially in developing countries with shortage of diagnostic kits, as well as developed countries with limited quantity of kits (15). In our study, there were 5 cases with negative HRCT results and positive RT–PCR, among whom 4 cases were finally diagnosed as positive COVID–19. Negative HRCT results with positive RT–PCR has been also reported previously (22) and some suggest exclusion of HRCT from diagnostic criteria (23, 24). Also, two of the three patients who were diagnosed as not having COVID–19 had positive chest HRCT results at admission, which disappeared by repetition of this test and resulted in ruling out COVID–19 in these patients, which showed the false positive HRCT results. Therefore, we stand the point that the results of HRCT cannot be used for definite diagnosis of COVID–19 and the diagnosis of COVID–19 should be based on comprehensive evaluation of patients' conditions.

The results of RT–PCR and HRCT after the treatment are also of note; in addition to 3 cases with negative RT–PCR results and 4 cases with initial positive RT–PCR and negative post–treatment results (which showed the efficacy of treatment), there were 4 cases with initial negative RT–PCR, which became positive in the 2nd examination. This finding confirmed the results of previous studies on latency in positivity of RT–PCR of infected patients and late clearance of the test after treatment and discharge (25). Furthermore, among patients with positive HRCT results at admission, 9 cases became negative after the treatment and 7 ones remained positive. This finding showed that HRCT was not an appropriate tool for assessing the response to treatment (22).

According to the national guidelines, we perform RT–PCR and chest HRCT for all patients who refer to the hospital (26). But this approach may not be the most appropriate one, as some patients will flee from the hospital and do not give consent for undergoing this tests, in addition to the fact that HRCT exposes the patient to radiation and has several contraindications and cannot be performed for all patients (27). Therefore, we believe

that performing HRCT is not practical in all patients and cannot be performed as a screening method for any patient who enters the hospital. Furthermore, considering the risk of false negative results, it is necessary to follow the recommendations of personal protective equipment (PPE), regardless of the test results, especially the health care staff (28, 29).

In conclusion, this study showed that none of the suggested diagnostic tests, namely RT–PCR for COVID–19 nucleic acid or chest HRCT can result in definite diagnosis of COVID–19 and it is not an appropriate approach to perform both of these tests for screening COVID–19 in any patient who refers to the hospital; thus, we suggest that comprehensive evaluation of patients' conditions is required for the definite diagnosis of this pandemic disease, bearing in mind that the health care staff should follow the precautions and PPE, regardless of the test results. More extensive research is required in this regard.

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