Radiology

Efficacy of Chest CT for COVID-19 Pneumonia in France

Original Research

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Summary Statement

In France, chest CT in combination with reverse transcriptase-polymerase chain reaction (RT-PCR) testing was effective as a diagnostic tool to assess coronavirus disease 2019 (COVID-19) pneumonia in symptomatic patients.

Key Results

In a national survey of 26 hospitals (N= 4824 subjects), chest CT sensitivity and specificity for diagnosing COVID-19 pneumonia were 90% and 91%, respectively.

In 103 patients with an initial positive chest CT finding(s) for COVID-19 and a negative initial RT-PCR test, a repeat RT-PCR was positive in 90% (93/103).

In patients with both negative chest CT and RT-PCR, the negative predictive value regarding final discharge diagnosis for COVID-19 was 99% (2035/2050 patients).

Abbreviations:

CI - confidence interval

RT-PCR - Reverse Transcriptase - Polymerase Chain Reaction.

PPV - Positive Predictive Value

COVID-19 – Coronavirus disease 2019

Abstract

Background:

The role and performance of chest CT in the diagnosis of the coronavirus disease 2019 (COVID-19) pandemic remains under active investigation.

Purpose:

To evaluate the French national experience using Chest CT for COVID-19, results of chest CT and RT-PCR were compared together and with the final discharge diagnosis used as reference standard.

Materials and Methods:

A structured CT scan survey (NCT04339686) was sent to 26 hospital radiology departments in France between March 2 and April 24 2020. These dates correspond to the peak of the national COVID-19 epidemic. Radiology departments were selected to reflect the estimated geographical prevalence heterogeneities of the epidemic. All symptomatic patients suspected of having a COVID-19 pneumonia who underwent within 48 hours both initial chest CT and at least one RT-PCR testing were included. The final discharge diagnosis, based on multiparametric items, was recorded. Data for each center were prospectively collected and gathered each week. Test efficacy was determined by using Mann-Whitney Test, Student's t-test, Chi-square test and Pearson's correlation. A p value <.05 determined statistical significance.

Results:

Twenty-six of 26 hospital radiology departments responded to the survey with 7500 patients entered; 2652 did not have RT-PCR results or had unknown or excess delay between RT-PCR and CT. After exclusions, 4824 patients (mean age 64, ± 19 yrs, 2669 males) were included. Using final diagnosis as the reference, 2564 of the 4824 patients were positive for COVID-19 (53%). Sensitivity, specificity, NPV and PPV of chest CT for diagnosing COVID-19 were 2319/2564 (90%, 95% confidence interval [CI]: 89, 91), 2056/2260 (91%, 95%CI: 91, 92%), 2056/2300 (89%, 95%CI; 87, 90%) and 2319/2524 (92%, 95%CI 91, 93%) respectively. There was no significant difference for chest CT efficacy among the 26 geographically separate sites, each with varying amounts of disease prevalence.

Conclusion:

Use of chest CT for the initial diagnosis and triage of suspected COVID-19 patients was successful.

Introduction:

To date, over 15 million confirmed coronavirus disease 2019 (COVID-19) cases have been diagnosed and 671,000 people have died. Since its emergence in Asia late last year, the virus has spread to every continent except Antarctica. It is essential to detect this disease at its earliest stage and immediately isolate the infected person to limit its spread. According to several recommendations (1–3), the reference method for diagnosing COVID-19 is the reverse transcription polymerase chain reaction (RT-PCR) assay. However, RT-PCR has some limitations, such as quality of the sample collection and kit performances, which vary by manufacturer. RT-PCR is reported to have high specificity but variable sensitivity ranging from 60 to 70% (4) to 95-97% (5). A recent meta-analysis reported that RT-PCR testing had a pooled sensitivity of 89% (6). As a result, the false negative rate is a practical problem and it is recommended that several negative tests be obtained before being confident about excluding the disease. In the context of this epidemic, the low sensitivity of RT-PCR implies that many patients with COVID-19 may not be identified and consequently may not be isolated from healthy population. These individuals could continue to spread this disease. Chest CT can detect some characteristic features in almost all patients with COVID-19 pneumonia (7–9). These features have also been observed in patients with negative RT-PCR results but with clinical symptoms (10). In a recent meta-analysis, including 5 studies, Kim et al (6) reported pooled sensitivity of 94% (95% CI: 91%, 96%) for chest CT and 89% (95% CI: 81%, 94%; I2=90%) for RT-PCR. Pooled specificity for chest CT was 37% (95% CI: 26%, 50%).

Recent studies have reported good performance of Chest CT for the diagnosis of COVID-19 pneumonia (6, 15). However, chest CT can be normal, especially in the early course of the disease.

In this study, we hypothesized that chest CT has been effective as a primary diagnosis tool in clinical practice given the perceived higher sensitivity of Chest CT compared to the first RT-PCR test during the workup for the first hospital admission. To demonstrate that point, we launched a French national observational survey (11) to determine the efficacy of chest CT for the diagnosis of COVID 19 pneumonia. The final discharge diagnosis based on a multi-parametric item including clinical findings, RT-PCR testing, chest CT imaging, risk level of exposure, local estimated prevalence and biological data, was used as reference standard. Results of chest CT and RT-PCR were compared together and with the final discharge diagnosis.

Materials and Methods

The survey design was approved by the local institutional review board and recorded on the clinicaltrial.gov website (NCT04339686). Written informed consent was waived due to retrospective anonymized data collection.

Survey and Data Collection

A prospective survey was conducted from March 2 - April 24, 2020 corresponding to the French national COVID-19 epidemic peak. The survey was sent to 26 radiology centers, 14 university hospitals and 12 general hospitals, selected to reflect the geographic prevalence of COVID-19.

The level of epidemic prevalence was estimated each week by the French national health care administration and classified for this study in three types: under 20%, between 20 and 30% and between 31 and 40%.

To reflect potentially different management patterns, four university and public hospitals per geographic area were randomly chosen. Two university hospitals from areas with estimated low disease prevalence were also solicited to balance the national mean prevalence.

For each center, a weekly survey was sent to a referent senior radiologist. The survey included the following parameters: clinical patient data (age, sex), results of initial chest CT and initial and/or repeat RT-PCR tests, time intervals between chest CT and RT-PCR, and final discharge summary according to the hospital discharge report. All patients having undergone both chest CT scan and RT-PCR for suspected COVID-19 were eligible for the survey.

All data were retrieved by manual data extraction from electronic hospital medical records by the referent radiologist.

CT Protocol and Image Analysis

CT examinations were established in accordance with the international guidelines and the local references and are given in Appendix E1 along with an enumeration of the RT-PCR test kits used (Appendix E2).

For each center, a first reading of the presenting chest CT was performed by a single on-site senior radiologist with at least 5 years of experience in emergency radiology. In cases of doubt or difficulties, a double reading was performed in consensus with second reader with ≥5 years of experience in thoracic imaging. Each reader was blinded to the RT-PCR result, but aware of suspicion for COVID-19. Years of experience of the readers is provided in Appendix E1.

A dedicated reading grid, the Rad Report issued by the RSNA, translated in French, was used for each reading (12). According to this structured report, typical findings included:
Bilateral ground glass opacities with peripheral distribution, bilateral crazy paving appearance with intralobular thickening, reverse halo sign, or other signs compatible with organizing pneumonia. The presence of at least one of these findings was associated with strong COVID-19 suspicion. Normal Chest CT findings and atypical patterns such as mediastinal lymphadenopathy, pleural effusion, multiple tiny pulmonary nodules, tree-in-bud nodules, and cavitation (1, 13, 14) were classified as negative for COVID-19.

RT-PCR Testing

The RT-PCR assay were performed for each patient. Complete description is given in Appendix E2. Qualitative detection of nucleic acid from SARS-CoV-2 was performed using deep oropharyngeal sampling in all 26 centers. If results of the initial RT-PCR test were negative, results of repeat RT-PCR were recorded. We considered that three negative RT-PCR tests within 6 days were indicative of a negative COVID-19 diagnosis. We considered that a positive diagnosis for COVID-19 infection was present when one was found. Patients with more than 48 hours between chest CT and the initial RT-PCR and those for whom the delay between RT-PCR assay and chest CT was not mentioned were excluded from the analysis.

To evaluate the clinical practice, results of chest CT and RT-PCR were compared together and with the final discharge diagnosis used as reference standard. The final discharge diagnosis was based on multiparametric items, risk level of exposure, local estimated prevalence, symptoms (fever, cough, fatigue, dyspnea, anosmia), evolution during hospitalization for inpatient,

lymphopenia, low C-reactive Protein, high procalcitonin, Chest CT and initial and repeated RT-PCRs.

Statistical Analysis

Standard data analysis was performed by a data scientist (M.N, 10 years of experience) using a three-step method: (a) automatic data collection using Microsoft Form (Redmond, Washington, USA), (b) data cleaning and indexing upon identification data using Python Data Analysis Library 1.0.3 (AQR Capital Management, Lambda Foundry, Inc.) and (c) manual extraction of data.

The algorithm to assess diagnosis was established considering RT-PCR results and final discharge summary (secondary end point).

Because the cohort in our survey was not derived from random selection, all statistics are deemed descriptive. No imputation was made for missing data. Continuous variables are expressed as medians and simple ranges. A 95% confidence interval (CI) was obtained with the Wilson score method. Categorical variables are summarized as counts and percentages. Diagnostic accuracy, including sensitivity, specificity, PPV, negative predictive value, and accuracy of chest CT imaging, were calculated using final report as the reference standard. Associations were studied using Student t test. All analyses were performed with R software, version 3.6.2 (R Foundation for Statistical Computing, 2010).

Results

Demographic Results

Twenty-six of 26 hospital radiology departments responded to the survey, corresponding to 7500 patients. The study flow chart is given Figure 1. Among the 7500 patients, 2652 were secondarily excluded because either they had no RT-PCR results (n = 57) or because there was an excessive or unknown delay between RT-PCR and CT (n = 2619). Finally, 4824 patients were included. Mean age (±standard deviation) was 63.9 years ± 18.9 [3, 101 years], including 2155 females (45%) and 2669 males (55%). Among them, there were significantly more male than female patients with positive findings at both chest CT and RT-PCR (p = 0.03). The time interval between chest CT and RT-PCR was less than 24 hours for 54.5% (4088 / 4824) of patients, and between 24 and 48 hours for 10% (796/4824) of patients. Table 1 summarizes the demographic and clinical characteristics of the study population. Fifty-four percent of patients were from geographic areas with estimated disease prevalence of less than 20% (2605 / 4824). In 53% of cases (2575/4824), the initial RT-PCR result was negative.
Estimated prevalence of the disease over the duration of the study is shown in Appendix E2.

The diagnosis algorithm used to assess COVID-19 pneumonia in our survey is provided in Figure E1.

Analysis considering the final diagnosis according to the Hospital discharge report.
By considering the final diagnosis from the hospital discharge report, sensitivity and specificity of chest CT scan were 90% (95%CI; 88, 91; 2320/2564) and 91% (95%CI; 90, 92; 2056/2260) respectively.

With mean estimated prevalence of 20%, the calculated positive predictive value (PPV) was 92% (95%CI; 91, 93; 2320 /2524) and negative predictive value (NPV) was 89% (95%CI; 87, 90; 2056 /2300).

There were no significant differences in the sensitivity of chest CT regardless of geographic disease prevalence (91% in low prevalence area, 86% in intermediate and 89% in high prevalence, p = .14). PPV and sensitivity of chest CT were higher in the male population than in the female population (91% for the male patients, 85% for the female, p = 0.02).

With regard to the final discharge report, 24 RT-PCR samples were false positive (0.005%, 24/4824). The Negative predictive value for RT-PCR was 87% (95% CI; 85, 90; 2236/2575).

According to this survey, 2035 patients had both negative RT-PCR and Chest CT, 202 patients with negative initial RT-PCR and other parameters suggestive of negativity and 6-day follow-up. 10 Patients with at least 2 negative repeated RT-PCR during the 6 days follow When findings for both chest CT and RT-PCR were negative, the negative predictive value regarding final discharge summary was 99% (95% CI: 99, 100, 2035 of 2050 patients).

Table 2 illustrates the performances of Chest CT and RT- PCR performances using the Final discharge summary as the reference standard. Chest Ct performances with regard to geographic prevalence and considering the final discharge summary as reference for each centers are provided in Table E1. Overall chest CT performances with initial RT-PCR as the reference standard and according to age, sex, and geographic prevalence are provided in Appendix E5.

Discussion

This study reports a nationwide survey on the role of Chest CT in initial assessment of COVID-19 pneumonia. We demonstrate that, in clinical practice, RT-PCR and chest CT were used simultaneously for medical triage whatever the hospital's expertise level and estimated

prevalence for COVID-19. Twenty-six of 26 hospital radiology departments responded to the survey. 4824 patients were included for this analysis. Using the final discharge report as the reference standard, 2564 of the 4824 patients were positive for COVID-19 (53%). Sensitivity, specificity, NPV and PPV of chest CT for diagnosing COVID-19 were 90% (95% CI; 89, 91), 91% (95% CI; 91, 92), 89% (95% CI; 87, 90) and 92% (95% CI; 91, 93) respectively. There was no significant difference for chest CT efficacy among the 26 geographically separate sites, each with varying amounts of disease prevalence.

For COVID 19, sensitivity and specificity of RT-PCR and Chest CT remains debated; in cases of low disease prevalence (<10%), the positive predictive value of RT-PCR was reported to be ten-fold that of chest CT (16). In cases involving a wide range of prevalence, pooled 94% sensitivity and 37% specificity were reported for RT-PCR in a recent meta-analysis (6).

Thus, the results of this study are in contrast to recommendations for CT use; indeed, for a large majority of them, using CT as a screening tool is actually discouraged (1–3,15) while others recommend it suggest CT as a surrogate diagnostic test (1,13). Whatever the debate, all of them recommend RT-PCR as the reference diagnosis method. In a recent publication dated April 7, 2020 (17), a Fleischner Society consensus stated that imaging is not indicated in cases of suspected COVID-19 with mild clinical symptoms except in cases of disease progression. On the other hand, the Fleischner Society recommends imaging for medical triage in patients suspected of having COVID-19 who present with moderate to severe clinical symptoms and a high pretest probability of disease. This statement was put forward to limit imaging resource over-using, to decrease risk of viral transmission to radiology staff and patients and to consider additional ionizing radiation exposure (15).

The second message of this study is that in clinical practice, final diagnosis of COVID-19 was sometimes made without any positive RT-PCR tests, since in the large majority of COVID patients, only one RT-PCR assay was performed. This is not altogether in compliance with the international recommendations. For these patients, final diagnosis was made from multiparametric criteria; evolution of clinical symptoms, compatible CT findings, and biological ancillary criteria such as lymphopenia, increased prothrombin time, increased lactate dehydrogenase, and/or mild elevations of inflammatory markers (20). Notwithstanding its relative low sensitivity, RT-PCR has the disadvantage of providing delayed results, often in several hours, and its performance could depend on variations in detection rates from different manufacturers, variations due to patient viral load, and/or improper clinical sampling. In addition, Chest CT presents two main interests: the test is available immediately and results are available in fewer than 15 minutes even if imaging features of COVID-19 pneumonia are non-specific, sometimes overlapping with other viral pneumonias (18,19). In a context of spreading epidemic, limits of RT-PCR and advantages of CT, could explain the atypical diagnosis algorithm observed here.

Our survey demonstrates that, whatever the severity of the symptoms, in areas of relative high prevalence, in clinical practice, RT-PCR and chest CT were used simultaneously for medical triage. There are some likely reasons; 1) early data from China suggests relatively poor diagnostic sensitivity of RT-PCR (16) and CT could additionally aid the clinician in patient triage; 2) In a pandemic, the risk of false-negative test results increases with the widespread character and the prevalence of the disease. The sensitivity of CT for COVID-19 pneumonia is debated but was recently estimated higher than RT-PCR by Fang Y et al (16), 91% versus 71% respectively ($p<.001$) and 90% versus 87% ($p = 0.04$) in our study. The sensitivity of the RT-

PCR affects the timely management of suspected cases (isolation and medical treatment) and furthers the risks of transmission.

In this study, the final diagnosis was based on a combination of parameters such as level of exposure, local prevalence, clinical evolution, compatible CT findings, RT-PCR testing and biological ancillary criteria such as lymphopenia, increased prothrombin time, increased lactate dehydrogenase and or mild elevations of inflammatory markers (20). The reference standard for COVID-19 infection is RT-PCR positivity, but this test does have false negatives.

Our results have limitations: First, the clinical data were limited (e.g., severity status was not precisely recorded). This factor-limited analysis regarding severity, some patients could have been severe, and others moderate to symptomatic. Therefore, it is difficult to state definitively on clinical practice for this criterion since we do not know precisely to whom the study applied. Second, different radiologists read chest CT images without centralized re-reading and reader experience could have introduced bias. Third, the imaging findings used to differentiate typical from atypical and/or normal findings could be debated. Chest CT protocols were not fixed, which could be associated with reading bias. For instance, it has been shown that contrast material injection may influence the interpretation of ground-glass opacity patterns (1). Fourth, approximately one-third of patients were excluded. Fifth, even if CT reading was performed without knowledge of RT-PCR results, chest CT readers were, aware that the patient was suspected for COVID-19. Lastly, disease prevalence evaluated by local French authorities could be not representative. In France, only symptomatic patients and a small proportion of asymptomatic exposed workers (including health workers, childcare workers) were tested for COVID-19 using RT-PCR. Because the whole population was not systematically screened, the disease prevalence used in this study were estimated. This could explain why performance of

chest CT was similar regardless of the disease prevalence, which is surprising since prevalence is supposed to have impact on the predictive values according to Bayes' theorem.

In conclusion, the results of this French national survey shed light on the role of chest CT in the current COVID-19 pandemic as an initial diagnostic tool in areas of relatively high disease prevalence. These data need to be considered during planning for either local hospital or national budget cycle.

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FIGURE

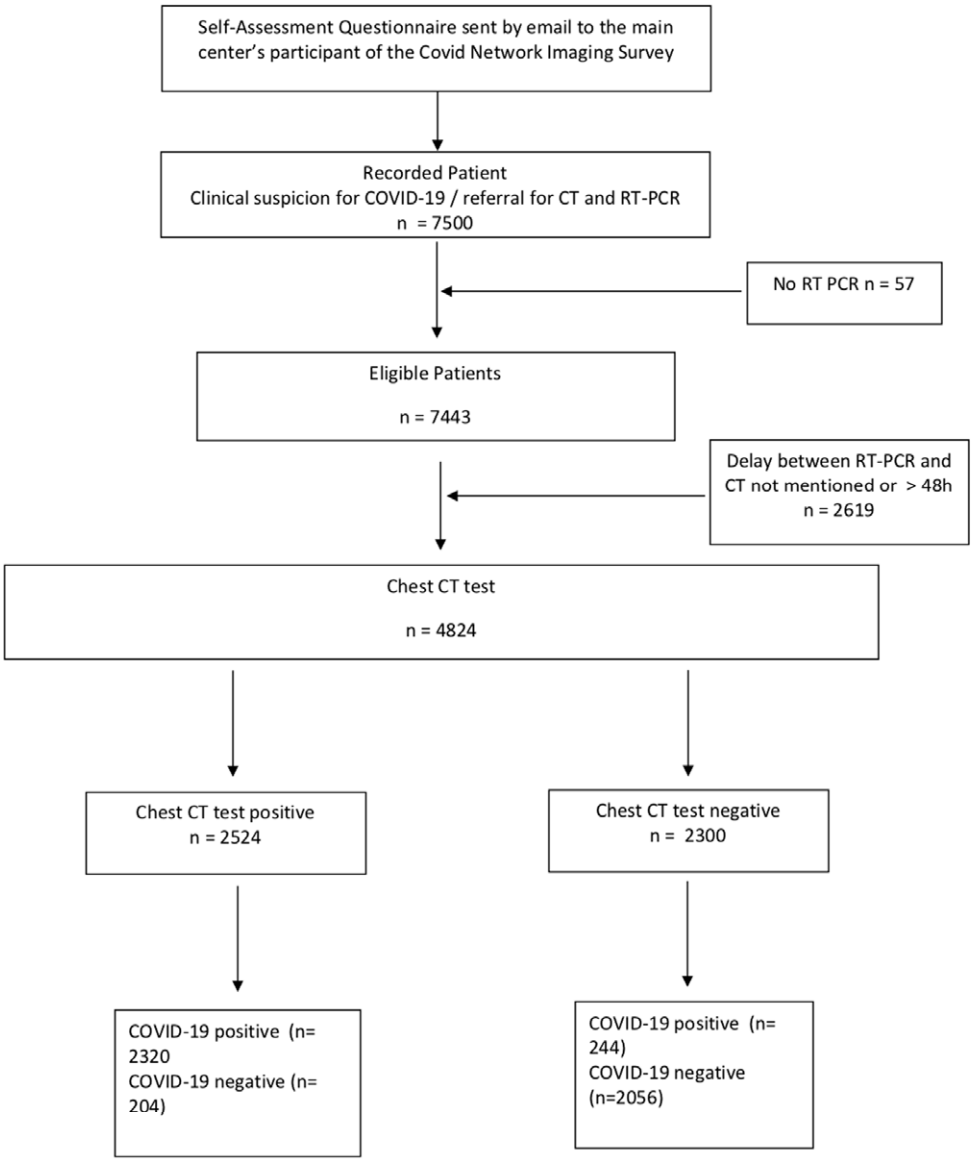

Figure 1. Flowchart of the study patients.

Figure 1. Flowchart of the study patients.

TABLES

Table 1

Parameter		Overall	Positive Chest CT	Negative Chest CT	*P* Value
No. of patients	n	4824	2249	2575	0.18
Mean Age (y)	Mean ± SD	64 ±19	65 ± 17	63 ± 21	0.14
Sex	M	2669	1492	1177	0.04
	F	2155	904	1251	0.03
Time delay between initial RT-PCR and Chest CT	<24h	4088	2152	1931	0.07
	24-48h	796	400	396	0.25
Geographic Prevalence	20% <	2605	1042 (40%)	1563 (60%)	0.009
	20%-30%	965	502 (52%)	463 (48%)	0.17
	31%-40%	1254	803 (64%)	451 (36%)	0.04

The demographic characteristics of the study population subjects and statistical differences within the subgroups. Note the time delay between when the first CT exam was performed and when the results of the first RT-PCR were available (in bold).

Table 2

	TP	TN	FP	FN	Sensitivity (%)	Specificity (%)	Positive predictive value %)	Negative predictive value (%)	Accuracy (%)
First Chest CT	2319	2056	204	245	90 [89,91] (2319/2564)	91 [91,92] (2056/2260)	92 [91,93] (2319/2524)	89 [87,90] (2056/2300)	90 [90,91]
First rt-PCR	2225	2236	24	339	87 [86,89] (2225/2564)	99 [98,100] (2236/2260)	99 [99, 100] (2225/2249)	87 [85,90] (2236/2575)	97 [96,97]
P* value					0.04	0.01	0.008	0.12	0.03

Table 2 illustrates the test efficacy for those research subjects that had both a chest CT and rt-PCR on admission using the final discharge diagnosis as the reference standard. TP : True Positive. TN : True Negative. FP : False Positive. FN : False Negative. [N, N]: Numbers in brackets are 95% Confidence Intervals (N,N) : Numbers in parentheses are raw data used to calculate percentages.

***P* value for difference between CT and rt-PCR**

Table 3

	5 hospitals with lowest prevalence First Chest CT	5 hospitals with highest prevalence First Chest CT	5 hospitals with lowest prevalence First rt-PCR	5 hospitals with highest prevalence First rt-PCR
Mean Prevalence Percentage	8	34	8	34
Number of Patients	796	1384	796	1384
Sensitivity (%)	87 [85,88] (186 / 213)	91 [90,92] (880 / 964)	89 [87,92] (189 / 213)	87 [86,87] (834/964)
Specificity (%)	90 [88,92] (523 / 582)	95 [93,96] (397 / 420)	99 [99,100] (581 / 582)	100 [99,100] (420 / 420)
Positive predictive value (%)	76 [73,78] (186/245)	97 [95,98] (880/903)	98 [97,99] (189/193)	99 [99,100] (834/842)
Negative Predictive Value (%)	95 [94,96] (523/551)	82 [81,84] (397/481)	96 [94,97] (581/603)	77 [76,79] (420/542)
Accuracy %)	90	94	98	96

Efficacy of Chest CT and RT-PCR compared to final Discharge summary as Reference Standard, comparing the five hospitals with the lowest prevalence to the five hospitals with the highest prevalence of COVID-19 infection. The estimated prevalence for symptomatic COVID-19 pneumonia are respectively for the lowest five hospitals 8% and 34% for the highest five hospitals. [N, N]: Numbers in brackets are 95% Confidence Intervals. (N,N) : Numbers in parentheses are raw data used to calculate percentages.

Appendix E1

Individuals participating at the study and years of experience in emergency and thoracic imaging

G.H, 6 years of experience; M.L, 15 years of experience; M.O, 15 years of experience; K.C, 15 years of experience; G.J., 6 years of experience; C.F, 5 years of experience; C.D.M, 5 years of experienc; L.M, 2 years of experience; I.F, 11 years of experience; A.J, 15 years of experience; P.A 12 years of experience; I.P, 8 years of experience; O.B, 20 years of experience; A.C, 10 years of experience; M.M, 2 years of experience; G.H, 4 years of experience; P.G, 2 years of experience; M.G, 8 years of experience; E.B, 10 years of experience; B.L, 4 years of experience; A.K, 3 years of experience; F.D, 5 years of experience; B.D, 10 years of experience.

Appendix E2

Geographic prevalences and exclusion rate

Center reference	Patients (n)	Patients finally analyzed (n)	Exclusion rate (%)	Geographic estimated prevalence
1	790	612	23	34
2	177	163	8	34
3	202	197	2	14
4	504	247	51	8
5	329	325	1	8
6	216	216	0	10
7	151	128	15	14
8	1379	977	29	24
9	430	408	5	10
10	240	40	83	8
11	818	38	95	27
12	284	174	39	27
13	62	27	56	9
14	102	89	13	10
15	120	97	19	14
16	195	177	9	8
17	238	156	34	10
18	121	75	38	34
19	210	209	0	34
20	225	2	99	34

21	32	6	81	8
22	130	41	68	8
23	3	2	33	8
24	428	325	24	34
25	17	1	94	27
26	97	92	5	10

Appendix E3

Chest CT protocol

CT examinations were performed using the following parameters: slice thickness between 0.6 mm to 1.25 mm, mean pitch: 1.36 (± 0.3 [0.8,2]; mean tube voltage range 120kvP (± 35 [80,140]); automated mAs modulation. Mean radiation doses were 160 mGy.cm (± 40 [80, 400]).

Appendix E4

Reverse transcriptase Polymerase Chain Reaction and CT devices.

Some centers had multiples devices, therefore there are 32 registered answers.

Idx Centre	Rt-Pcr Devices	CT Devices
1	Thermocycleur Roche Diagnostic	Ge Revolution Evo (2018) -1
54	Abbott, Elitech, Roche Diagnostics	Ge Revo Evo 64 Ge Revo Evo 64
59	Thermocycleur Roche Diagnostic	Canon Aquilion Prime Sp Canon Aquilion One Prism Canon Aquilion One Genesis
98	Roche Diagnostics : Light Cycler 480	GE Révolution Evo GE Discovery Ct 750 Hd
102	Seegene : Allplex 2019-Ncov Assay Extraction Sur Automate Nimbus Cfx96 Eurobio	Siemens Somatom Definition Edge - 1
111	Biorad - Pcr Temps Réel Cfx96 Bd - Pcr Temps Réel Bd Max Seegene - Pcr Multiplex Seegene Allplex	Siemens Edge (Juin 2019) - 1
121	Kit Allplex 2019-Ncov Assay Seegene	GE 750hd
123	Lightcycler 480 Instrument Ii (Roche)	GE Revolution Discovery
141	Na	GE Revolution Discovery
154a	Stepone (Thermofisher), Qs5 (Biomérieux) Et Qiastat (Qiagen)	GE Revolution Discovery
154b	Stepone (Thermofisher), Qs5 (Biomérieux) Et Qiastat (Qiagen)	Siemens Somatom

155a	Beckton Dickison : Automate Bd Max Avec Réactif Viasure Sars-Cov-2 S Gene (Certest) Beckton Dickison : Automate Bd Max Avec Réactif Anatolia Geneworks (Launchdiagnostics) Cepheid : Automate Gene Xpert Infinity System Avec Réactif Xpert® Xpress Sars-Cov-2 Ruo	Siemens Somatom Definition Edge
155b	Beckton Dickison : Automate Bd Max Avec Réactif Viasure Sars-Cov-2 S Gene (Certest) Beckton Dickison : Automate Bd Max Avec Réactif Anatolia Geneworks (Launchdiagnostics) Cepheid : Automate Gene Xpert Infinity System Avec Réactif Xpert® Xpress Sars-Cov-2 Ruo	Canon Aquilion Lightning
155c	Beckton Dickison : Automate Bd Max Avec Réactif Viasure Sars-Cov-2 S Gene (Certest) Beckton Dickison : Automate Bd Max Avec Réactif Anatolia Geneworks (Launchdiagnostics) Cepheid : Automate Gene Xpert Infinity System Avec Réactif Xpert® Xpress Sars-Cov-2 Ruo	Canon Aquilion Prime
161	Seegene / Rt-Pcr Triple Cible, Automates Nimbus and Starlet Double Cible Et Amplificateur Abbott and Réactif Biomérieux (Double Cible) Et Film-Array	Siemens Edge 64b/128 Coupes
218	Machine Pcr Genexpert (Société Cepheid) Kit Xpert Xpress Sars-Cov-2	GE Revolution Hd
225	Cfx96 Thermocyclers (Bio-Rad)	GE Optima 540ct ,
225	Cfx96 Thermocyclers (Bio-Rad)	Canon Aquilion Prime Sp

237	Extraction Easymag Ou Emag (Biomerieux) Amplification Cfx 96 (Biorad) Technique Cnr Ou Genefinder Ou Viasure Ou Argene	Toshiba Aquillion 16
237	Extraction Easymag Ou Emag (Biomerieux) Amplification Cfx 96 (Biorad) Technique Cnr Ou Genefinder Ou Viasure Ou Argene	GE Revolution Evo
237	Extraction Easymag Ou Emag (Biomerieux) Amplification Cfx 96 (Biorad) Technique Cnr Ou Genefinder Ou Viasure Ou Argene	GE Revolution Evo
237	Extraction Easymag Ou Emag (Biomerieux) Amplification Cfx 96 (Biorad) Technique Cnr Ou Genefinder Ou Viasure Ou Argene	GE Revolution Evo
243	Automate Roche	GE Discovery Revolution Hd GE Optima 660
243	Automate Roche	GE Optima 660
289	Allplex 2019-Ncov Assay – Seegene Sur Cfx 96 (Biorad) Xpert Xpress Sars-Cov-2 Assay – Cepheid Sur Genexpert	Canon Aquilion Prime 128 Canon Aquilion Prime 128
367	Abbott M2002	Siemens Somaton Définition As
424	Cobas Sars-Cov-2 (Roche)	Canon Aquilion Prime
474	1 Scanner Révolution Evo De Chez Ge	
481	Automate Panther Fusion® (Hologic, Usa)	GE Revolution Gsi Philips Ict 256 Philips Ingenuity Ct Siemens Somatom Definition As Siemens Somatom Definition As+ Canon Aquilion Lightning
243 Bis	Automate Roche	GE Discovery Revolution Hd GE Optima 660 S

Appendix E5

Analysis with RT-PCR as reference standard

In 53% of cases (2575/4824), the initial RT-PCR result was negative. Among them, 525 had positive chest CT scans showing typical imaging findings and 103 (18%, 103/525) underwent repeat RT-PCR assay (second and/or third if the second test was negative). Positive result of repeat RT-PCR was observed in 93 of the 103 patients (90%). For the 422 remaining patients (80%, 422/525) with negative findings at initial RT-PCR and positive findings at chest CT, RT-PCR was not repeated. Considering RT-PCR as gold standard, sensitivity and specificity of chest CT for diagnosing COVID-19 were 0.80 (95% confidence interval [CI]: 0.79, 0.81), 0.88 (95%CI: 0.86-0.90) respectively.

With a mean estimated prevalence of 20%, the positive predictive value (PPV) was 79% (95% CI: 78,81; 1999 of 2524 patients) and negative predictive value was 89% (95% CI: 87,90; 2050 of 2300 patients).

Table E1

Center reference	Geographic prevalence	Number of Patients	TP	TN	FP	FN	Sensitivity (%)	Specificity (%)	Positive Predicted Value (%)	Negative Predicted Value (%)
1	34	612	370	201	0	40	90	100	100	84
2	34	163	104	55	1	3	98	98	99	97
3	14	197	81	86	16	14	86	84	84	87
4	8	247	44	176	16	11	83	92	73	95
5	8	325	86	211	21	6	96	91	80	98
6	10	216	114	87	3	12	92	97	97	90
7	14	128	70	42	7	9	89	86	91	82
8	24	977	483	369	47	78	87	89	91	83
9	10	408	169	231	3	6	98	99	98	98
10	8	40	40	0	0	0	100	0	100	0
11	27	38	15	19	3	1	94	86	83	95
12	27	174	45	94	23	12	79	80	66	89
13	9	27	6	14	7	0	100	67	46	100
14	10	89	40	44	4	1	98	88	88	98
15	14	97	36	56	2	3	92	97	95	95
16	8	177	38	120	15	4	93	89	72	98
17	10	156	129	12	2	14	92	86	98	50
18	34	75	31	22	22	0	100	50	59	100
19	34	209	176	20	0	13	93	100	100	61
20	34	2	1	1	0	0	100	100	100	100
21	8	6	5	0	1	0	100	0	83	0
22	8	41	13	16	6	6	68	73	68	73
23	8	2	1	1	0	0	100	100	100	100
24	34	325	199	99	0	27	89	100	100	80
25	27	1	1	0	0	0	0	0	0	0
26	10	92	22	59	5	6	88	93	81	95
Total		**4824**	**2319**	**2035**	**204**	**266**	**90 [89,91] (2319/2564)**	**91 [81,83] (2056/2260)**	**92 [91,93] (2319/2524)**	**89 [87,90] (2056/2300)**

Table E1 illustrates the Prevalence and Chest CT performance by hospital center number with final discharge summary as reference. Numbers in brackets are 95% Cis, and numbers in parentheses are raw data used to calculate percentages. TP : True Positive. TN : True Negative. FP : False Positive. FN : False Negative.

Table E2

Criteria	Value	No. of Patients (n)	TP	TN	FP	FN	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive P Value
Overall		4824	1999	2050	525	250	0.88% [0.86,-0.90] (1999/2249)	0.80% [0.79, - 0.81] (2050/2575)	0.79% [0.78, - 0.81] (1999/2524)	0.89% [0.87, - 0.90] (2050/2300)
Sex	F	2155	749	1072	201	133	0.85% [0.84,-0.87] (749/882)	0.84% [0.82,-0.86] (1072/1273)	0.79% [0.77,-0.81] (749/950)	0.88% [0.87,-0.90) (1072/1205)
	M	2667	1249	977	324	117	0.91% [0.89,-0.91] (1249/1366)	0.75% [0.72,-0.77] (977/1301)	0.79% [0.77,-0.80] (1249/1573)	0.89% [0.88,-0.90] (977/1154)
Age	<= 60	1926	769	849	203	105	0.88% [0.87-,0.90] (769/874)	0.81% [0.80,-0.83] (849 / 1052)	0.79% [0.78, - 0.81] (769/972)	0.89% [0.86, - 0.90] (849/954)
	>60	2898	1230	1201	322	145	0.89% [0.88,-0.91] (1230/1375)	0.79% [0.78,-0.80] (1201/1523)	0.79% [0.78,-0.81] (1230/1552)	0.90% [0.89,-0.91] (1201/1346)
Prevalence	< 20	2248	743	1164	264	77	0.91% [0.90,-0.92] (743/820)	0.82% [0.81,-0.83] (1164/1428)	0.74% [0.72,-0.76] (743/1007)	0.94% [0.93,-0.95] (1164/1241)
	20-30	1189	522	494	90	83	0.86% [0.83,-0.88] (522/605)	0.85% [0.83,-0.86] (494/584)	0.85% [0.84,-0.86] (522/612)	0.85% [0.84,-0.87] (494/577)
	30-40	1387	734	392	171	90	0.89% [0.88,-0.91] (734/825)	0.70% [0.68 ,- 0.71] (392/563)	0.81% [0.80, -0.82] (734/905)	0.81% [0.79,-0.84] (392/482)

Table E2 illustrates the Chest CT Performances compared with RT PCR as reference standard. NB : Numbers in brackets are 95% Cis, and numbers in parentheses are raw data used to calculate percentages. All percentages are with a 0.95 confidence interval. Data in parentheses are numbers of patients used to calculate percentages. TP : True Positive. TN : True Negative. FP : False Positive. FN : False Negative.

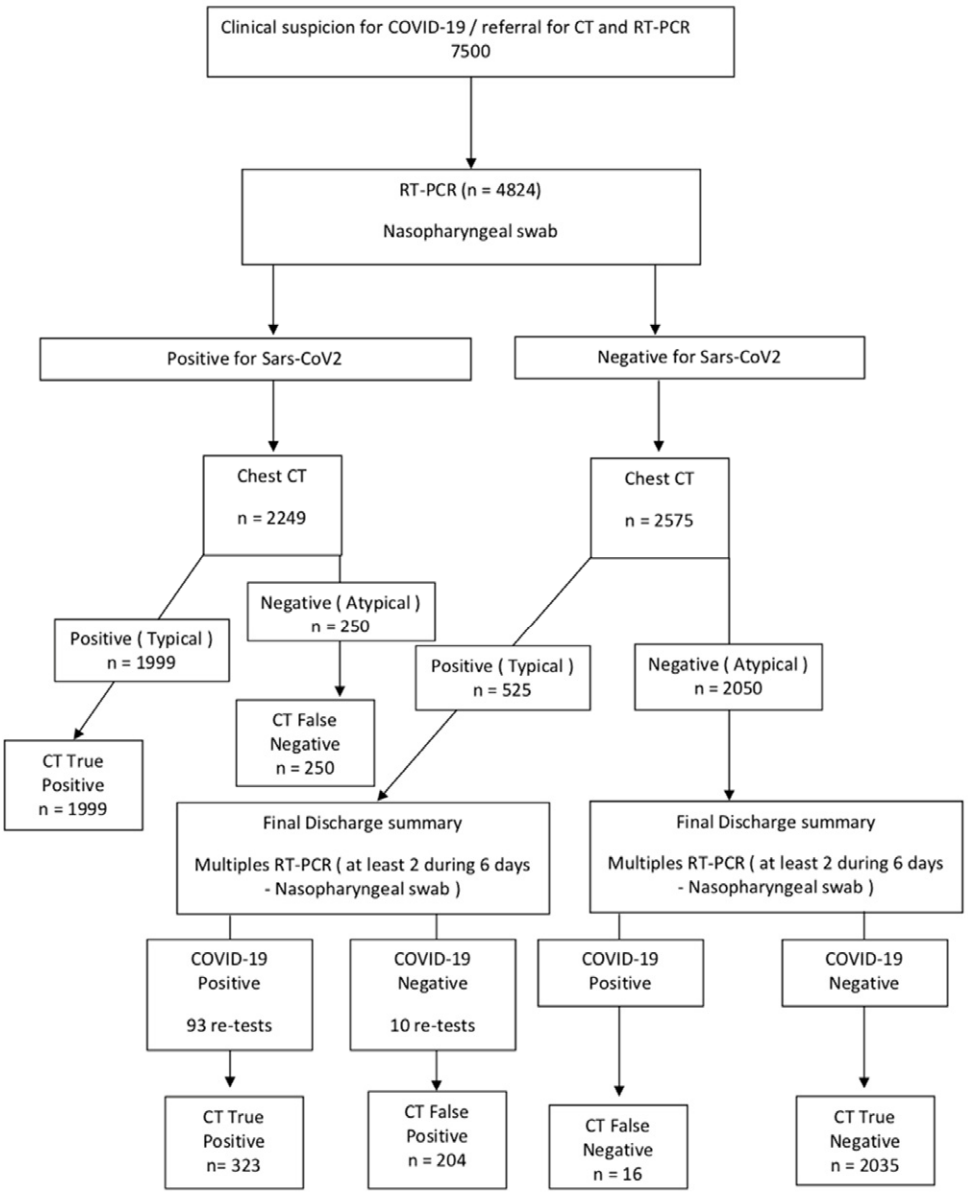

Fig 2. Flowchart illustrates the results from RT-PCR and chest CT for the survey patients. The diagnosis was determined by using the final discharge summary as the reference standard.

Figure E1. Flowchart illustrates the results from RT-PCR and chest CT for the survey subjects. The diagnosis was determined by using the final discharge summary as the reference standard.