Radiology

ORIGINAL RESEARCH • THORACIC IMAGING

Efficacy of Chest CT for COVID-19 Pneumonia Diagnosis in France

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Conflicts of interest are listed at the end of this article.

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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 reverse transcription polymerase chain reaction (RT-PCR) assays were compared together and with the final discharge diagnosis used as the reference standard.

Materials and Methods: A structured CT scan survey (NCT04339686) was sent to 26 hospital radiology departments in France between March 2, 2020, and April 24, 2020. These dates correspond to the peak of the national COVID-19 epidemic. Radiology departments were selected to reflect the estimated geographic prevalence heterogeneities of the epidemic. All symptomatic patients suspected of having COVID-19 pneumonia who underwent both initial chest CT and at least one RT-PCR test within 48 hours 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 the Mann-Whitney test, Student *t* test, χ^2 test, and Pearson correlation coefficient. $P < .05$ indicated a significant difference.

Results: Twenty-six of 26 hospital radiology departments responded to the survey, with 7500 patients entered; 2652 did not have RT-PCR test results or had unknown or excess delay between the RT-PCR test and CT. After exclusions, 4824 patients (mean age, 64 years ± 19 [standard deviation], 2669 male) were included. With final diagnosis as the reference, 2564 of the 4824 patients had COVID-19 (53%). Sensitivity, specificity, negative predictive value, and positive predictive value of chest CT in the diagnosis of COVID-19 were 2319 of 2564 (90%; 95% CI: 89, 91), 2056 of 2260 (91%; 95% CI: 91, 92), 2056 of 2300 (89%; 95% CI: 87, 90), and 2319 of 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 patients suspected of having coronavirus disease 2019 was successful.

Online supplemental material is available for this article.

Abbreviations

COVID-19 = coronavirus disease 2019, RT-PCR = reverse transcription polymerase chain reaction

Summary

In France, chest CT in combination with reverse transcription polymerase chain reaction testing was effective as a diagnostic tool in assessing coronavirus disease 2019 pneumonia in symptomatic patients.

Key Results

- In a national survey of 26 hospitals (4824 patients), chest CT specificity, sensitivity, negative predictive value, and positive predictive value in the diagnosis of coronavirus disease 2019 (COVID-19) pneumonia were 0.88 (95% CI: 0.86, 0.90), 0.80 (95% CI: 0.79, 0.81), 0.89 (95% CI: 0.87, 0.90), and 0.79 (95% CI: 0.78, 0.81), respectively.
- In 103 patients with initial positive chest CT findings for COVID-19 and a negative initial reverse transcription polymerase chain reaction (RT-PCR) test result, a repeat RT-PCR test was positive in 90% (93 of 103) of patients.
- In patients with negative chest CT and RT-PCR results, the negative predictive value regarding final discharge report for COVID-19 was 99% (95% CI: 99, 100 [2035 of 2050 patients]).

At the time of this writing, there were over 15 million confirmed coronavirus disease 2019 (COVID-19) cases, and 671 000 people had died. Since its emergence in Asia in late 2019, 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 assays have some limitations, such as quality of the sample collection and kit performances, which vary by manufacturer. The RT-PCR test is reported to have high specificity but variable sensitivity, ranging from 60%–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 results be obtained before one can be confident about excluding the disease. In the context of this epidemic, the low sensitivity of the RT-PCR assay implies that many patients with COVID-19 may not be identified and consequently may not be isolated from the healthy population. These individuals could continue to spread this disease. Chest CT can depict 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 clinical symptoms (10). In a recent meta-analysis that included five studies, Kim et al (6) reported pooled sensitivity of 94% (95% CI: 91, 96) for chest CT and 89% (95% CI: 81, 94; I^2 = 90%) for RT-PCR assays. Pooled specificity for chest CT was 37% (95% CI: 26, 50).

Recent studies have reported good performance of chest CT in the diagnosis of COVID-19 pneumonia (6,11). However, chest CT findings can be normal, especially in the early course of disease.

In this study, we hypothesized that chest CT has been effective as a primary diagnostic tool in clinical practice, given the perceived higher sensitivity of chest CT compared with that of the first RT-PCR test during the work-up for the first hospital admission. To demonstrate that point, we launched a French national observational survey (12) to determine the efficacy of chest CT for the diagnosis of COVID-19 pneumonia. The final discharge diagnosis based on multiparametric items, including clinical findings, RT-PCR testing, chest CT imaging, risk level of exposure, local estimated prevalence, and biologic data, was used as the reference standard. Results of chest CT and a RT-PCR assay were compared together and with the final discharge diagnosis.

Materials and Methods

The survey design was approved by the local institutional review board and was recorded on *ClinicalTrials.gov* (NCT04339686). Written informed consent was waived because of the retrospective anonymized data collection.

Survey and Data Collection

A prospective survey was conducted from March 2, 2020, to 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, which were 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: less than 20%, 20%–30%, and 31%–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 repeat RT-PCR tests, time between chest CT and RT-PCR assay, and final discharge summary according to the hospital discharge report. All patients who underwent both chest CT and an RT-PCR assay and were suspected of having COVID-19 were eligible for the survey.

All data were retrieved via 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 parameters are given in Appendix E1 (online). An enumeration of the RT-PCR test kits used is outlined in Table E1 (online).

For each center, a first reading of the initial chest CT images was performed by one 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 a second reader with 5 or more years of experience in thoracic imaging. Each reader was blinded to the RT-PCR result but was aware of suspicion for COVID-19

infection. Years of experience of the readers is provided in Appendix E2 (online).

A dedicated reading grid, RadReport *(https://radreport.org/)*, issued by the Radiological Society of North America and translated into French, was used for each reading (13). 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 suspicion for COVID-19. Normal chest CT findings and atypical patterns, such as mediastinal lymphadenopathy, pleural effusion, multiple tiny pulmonary nodules, tree-in-bud nodules, and cavitation (1,14,15), were classified as negative findings for COVID-19.

RT-PCR Testing

RT-PCR assays were performed for each patient. A complete description of this is given in Appendix E3 (online). Qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 was performed using deep oropharyngeal sampling in all 26 centers. If initial RT-PCR test results were negative, results of repeat RT-PCR tests were recorded. We considered that three negative RT-PCR tests within 6 days indicated a negative COVID-19 diagnosis. We considered 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 assay and those in whom the delay between the RT-PCR assay and chest CT was not mentioned were excluded from the analysis.

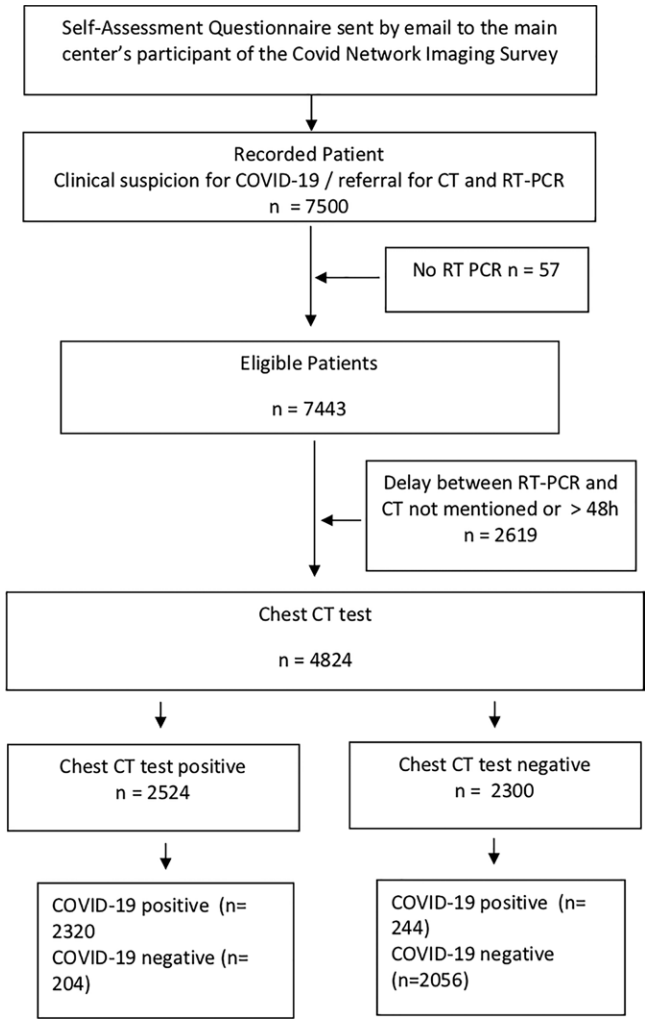
To evaluate the clinical practice, results of chest CT and RT-PCR assays were compared together, with the final discharge diagnosis used as the reference standard. The final discharge diagnosis was based on multiparametric items, risk level of exposure, local estimated prevalence, symptoms (fever, cough, fatigue, dyspnea, anosmia), progression of disease during hospitalization for inpatients, lymphopenia, low C-reactive protein level, high procalcitonin level, chest CT, and initial and repeated RT-PCR assays.

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 Forms (Microsoft), *(b)* data cleaning and indexing of identification data using Python Data Analysis Library (version 1.0.3; AQR Capital Management, Lambda Foundry), and *(c)* manual extraction of data.

The algorithm used to assess diagnosis was established considering RT-PCR results, and final discharge summary (secondary end point) is provided in Figure E1 (online).

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% CI was obtained with the Wilson score method. Categorical variables are summarized as counts and percentages. Diagnostic accuracy, including sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of chest CT imaging, were calculated using final reports as the reference standard. Associations were studied using the Student *t* test. All analyses were performed with R software, version 3.6.2 (R Foundation for Statistical Computing).



Flowchart of the study patients. COVID-19 = coronavirus disease 2019, RT-PCR = reverse transcription polymerase chain reaction.

Results

Demographic Results

All 26 hospital radiology departments responded to the survey, corresponding to 7500 patients. The study flowchart is given in the Figure. Among the 7500 patients, 2652 were secondarily excluded because they had no RT-PCR results (n = 57) or because there was an excessive or unknown delay between RT-PCR assays and CT (n = 2619). Finally, 4824 patients were included. Mean age was 63.9 years ± 18.9 (standard deviation) (age range, 3–101 years), and there were 2155 female (45%) and 2669 male (55%) patients. Among them, there were significantly more male than female patients with positive findings for both chest CT and RT-PCR assays (P = .03). The interval between chest CT and RT-PCR assay was less than 24 hours in 54.5% of patients (4088 of 4824) and between 24 and 48

Table 1: Demographic Characteristics of the Study Population and Statistical Differences Within Subgroups

Parameter	Overall	Positive Chest CT Findings	Negative Chest CT Findings	*P* Value
No. of patients	4824	2249	2575	.18
Age (y)*	64 ± 19	65 ± 17	63 ± 21	.14
Sex				
Male	2669	1492	1177	.04
Female	2155	904	1251	.03
Time delay between initial RT-PCR assay and chest CT				
<24 hours	4088	2152	1931	.07
24–48 hours	796	400	396	.25
Geographic prevalence†				
≤20%	2605	1042 (40)	1563 (60)	.009
21%–30%	965	502 (52)	463 (48)	.17
31%–40%	1254	803 (64)	451 (36)	.04

Note.—Unless otherwise indicated, data are numbers of patients. Notice the time delay between when the first CT examination was performed and when the results of the first reverse transcription polymerase chain reaction (RT-PCR) tests were available.

* Data are mean ± standard deviation.

† Data in parentheses are percentages.

Table 2: Test Efficacy in Patients Who Had Both Chest CT and RT-PCR Assay at Admission Using Final Discharge Diagnosis as the Reference Standard

Test	TP Result	TN Result	FP Result	FN Result	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 assay	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*	NA	NA	NA	NA	.04	.01	.008	.12	.03

Note.—Data in brackets are the 95% CI. Numbers in parentheses are raw data used to calculate percentages. FN = false-negative, FP = false-positive, NA = not applicable, RT-PCR = reverse transcription polymerase chain reaction, TN = true negative, TP = true positive.

**P* value for difference between CT and RT-PCR assay.

hours in 10% of patients (796 of 4824). 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 of 4824). In 53% of cases (2575 of 4824), the initial RT-PCR result was negative.

Estimated prevalence of the disease over the duration of the study is shown in Table E2 (online).

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

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 the chest CT scan were 90% (95% CI: 88, 91; 2320 of 2564) and 91% (95% CI: 90, 92; 2056 of 2260), respectively.

With a mean estimated prevalence of 20%, the calculated positive predictive value was 92% (95% CI: 91, 93; 2320 of 2524), and the calculated negative predictive value was 89% (95% CI: 87, 90; 2056 of 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 prevalence area, and 89% in high prevalence area; $P = .14$). Positive predictive value and sensitivity of chest CT were higher in the male population than in the female population (91% for male patients, 85% for female patients; $P = .02$).

With regard to the final discharge report, 24 RT-PCR assays yielded false-positive results (0.005%, 24 of 4824). The negative predictive value for RT-PCR assays was 87% (95% CI: 85, 90; 2236 of 2575).

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

Table 2 shows the performances of chest CT and RT-PCR assays using the final discharge summary as the reference standard.

Table 3: Efficacy of Chest CT and RT-PCR Assay Compared With Final Discharge Summary as Reference Standard

Parameter	Five Hospitals with Lowest Prevalence, First Chest CT	Five Hospitals with Highest Prevalence, First Chest CT	Five Hospitals with Lowest Prevalence, First RT-PCR Assay	Five Hospitals with Highest Prevalence, First RT-PCR Assay
Mean prevalence percentage	8	34	8	34
No. 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

Note.—Table compares data between five hospitals with the lowest prevalence and five hospitals with the highest prevalence of coronavirus disease 2019 (COVID-19) infection. The estimated prevalence data for symptomatic COVID-19 pneumonia are, respectively, for the lowest five hospitals 8% and 34% for the highest five hospitals. Data in brackets are 95% CIs. Data in parentheses are raw data used to calculate percentages. RT-PCR = reverse transcription polymerase chain reaction.

Chest CT performance with regard to geographic prevalence and considering the final discharge summary as the reference standard for each center is provided in Table E3 (online). Table 3 illustrates the different prevalences between five hospitals with the lowest prevalence and five hospitals with the highest prevalence of COVID-19 infection. Overall chest CT performances with the initial RT-PCR assay as the reference standard and according to age, sex, and geographic prevalence are provided in Table E4 (online).

Discussion

This study reports a nationwide survey on the role of chest CT in the initial assessment of coronavirus disease 2019 (COVID-19) pneumonia. We demonstrate that, in clinical practice, reverse transcription polymerase chain reaction assays 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. A total of 4824 patients were included in this analysis. Using the final discharge report as the reference standard, 2564 of the 4824 patients were positive for COVID-19 (53%). Sensitivity, specificity, negative predictive value, and positive predictive value 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 assays and chest CT continues to be debated; in cases of low disease prevalence (<10%), the positive predictive value of RT-PCR assays was reported to be 10-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 assays 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, use of CT as a screening tool is actually discouraged (1–3,11), whereas others who recommend it suggest CT be used as a surrogate diagnostic test (1,14). Whatever the debate, all agree with the recommendation of using RT-PCR assays as the reference method for diagnosis. In a publication dated April 7, 2020 (17), a Fleischner Society consensus stated that imaging is not indicated in patients suspected of having 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 overuse, to decrease risk of viral transmission to radiology staff and patients, and to consider reduction of additional ionizing radiation exposure (11).

The second message of this study is that in clinical practice, final diagnosis of COVID-19 was sometimes made without any positive RT-PCR test results because in a majority of patients with COVID-19, only one RT-PCR assay was performed. This is not altogether in compliance with international recommendations. In these patients, final diagnosis was made based on multiparametric criteria: evolution of clinical symptoms, compatible CT findings, and biologic ancillary criteria, such as lymphopenia, increased prothrombin time, increased lactate dehydrogenase level, and led to mild elevation of inflammatory markers (18). Notwithstanding its relative low sensitivity, RT-PCR assays have 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 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 nonspecific, sometimes overlapping with other viral pneumonias (19,20). In the context of a spreading epidemic, the limits of RT-PCR assays and the advantages of CT could explain the atypical diagnosis algorithm observed here.

Our survey shows that, whatever the severity of the symptoms, in areas of relative high prevalence and in clinical practice, RT-PCR assays and chest CT were used simultaneously for medical triage. There are some likely reasons: Early data from China suggest relatively poor diagnostic sensitivity of RT-PCR assays (16) and CT could additionally aid the clinician in patient triage. Furthermore, in a pandemic, the risk of false-negative test results increases with the widespread character and prevalence of the disease. The sensitivity of CT for COVID-19 pneumonia is debated but was recently estimated to be higher than that of RT-PCR assays by Fang et al (16), with sensitivity of 91% versus 71%, respectively ($P < .001$), and 90% versus 87% ($P = .04$) in our study. The sensitivity of the RT-PCR test affects the timely management of suspected cases (isolation and medical treatment) and furthers the risk 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 biologic ancillary criteria, such as lymphopenia, increased prothrombin time, increased lactate dehydrogenase level, or mild elevations of inflammatory markers (18). The reference standard for COVID-19 infection is positive findings of an RT-PCR assay, but this test does produce false-negative results.

Our study had some limitations: First, the clinical data were limited (eg, severity status was not precisely recorded). With this factor-limited analysis regarding severity, some patients could have had severe COVID-19 and others could have had moderate to symptomatic disease. Thus, it is difficult to state definitively on clinical practice for this criterion because we do not know precisely to whom the study applied. Second, different radiologists read chest CT images without centralized rereading, and reader experience could have introduced bias. Third, the imaging findings used to differentiate typical from atypical 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 of having COVID-19. Sixth, disease prevalence evaluated by local French authorities may not have been representative. In France, only symptomatic patients and a small proportion of asymptomatic exposed workers (including health workers and childcare workers) were tested for COVID-19 using RT-PCR assays. Because the whole population was not systematically screened, the disease prevalence data used in this study were estimated. This could explain why performance of chest CT was similar regardless of the disease prevalence, which is surprising because prevalence is supposed to have an impact on the predictive values according to the Bayes theorem.

In conclusion, the results of this French national survey shed light on the role of chest CT in the current coronavirus disease 2019 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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