Diagnostic performance of imaging tests for RT-PCR confirmed COVID19 and disease prevalence – initial results from a survey in the Netherlands

The Dutch COVID-imaging study group

Members are listed in alphabetical order

Annemarieke Bartels-Rutten, Ludo Beenen, Leonard Jan van Boven, Monique Brink, Pieter Cleyndert, Martijn Dirksen, HW van Es, Ansje Fortuin, Jim Geselschap, Hester Gietema, Martijn Gondrie, P.M. Huisman, Pim A. de Jong, Joost Kardux, Gerdien Kramer, Marc Kock, Arnoud Knoops, Emmeline Laupman - Koedam, Philip Linsen, Frank Looijmans, Lilian Meijboom, Julia Moelker-Galuzina, Arlette Odink, Jan Peringa, D.B. Piers, Milan Pijl, Jet Quarles van Ufford, N.S. Renken, Jan-Kees van Rooden, Annelie Slaar, Tessa Stigter-Jansen, Dominika Suchá, Marcela Spee-Drooková, Miranda Snoeren , Cornelia Schaefer-Prokop, Lauran Stöger, Hans Smeets, Steven Schalekamp, Jitske de Vries, Rianne Verhees, Rozemarijn Vliegenthart, HM Verkooijen, Jaap van Werkhoven, FJ Wesseling

Martini Ziekenhuis, Antoni van Leeuwenhoek Ziekenhuis, Tergooi Hilversum Blaricum, Franciscus Gasthuis & Vlietland, HagaZiekenhuis, LUMC, IJsselland Ziekenhuis, Amsterdam UMC locatie VUmc, Maasstad Ziekenhuis, Haaglanden Medisch Centrum, Albert Schweitzer Ziekenhuis, Ikazia Ziekenhuis, Ziekenhuis Gelderse Vallei, Amsterdam UMC locatie AMC, Isala Zwolle, Jeroen Bosch Ziekenhuis, OLVG, Ziekenhuis Rivierenland, Bernhoven Uden, Antonius Ziekenhuis Sneek, Groene Hart Ziekenhuis, Spaarne Gasthuis Haarlem, Radboudumc, Ziekenhuis Rijnstate, Meander Medisch Centrum, UMC Utrecht, Bravis ziekenhuis, Catharina Ziekenhuis, Reinier de Graaf ziekenhuis, Máxima Medisch Centrum, Albert Schweitzer Ziekenhuis, Erasmus MC, St. Antonius Ziekenhuis, MUMC+, ZGT / MRON, Medisch Centrum de Rivieren Zaandam, Dijklanderziekenhuis Hoorn, Gelre Apeldoorn, Zutphen, Martini Ziekenhuis, UMCG

Correspondence: Prof. dr. P.A. de Jong
University Medical Center Utrecht and Utrecht University
Heidelberglaan 100, 3584 CX Utrecht
Phone +31-887555555, E-mail: p.dejong-8@umcutrecht.nl

Introduction

During the rapidly evolving COVID19 pandemic continuous evaluation and, if needed, adaptation of diagnostic strategies is crucial. Most published studies concern retrospective (case) series from areas with high disease burden. Since positive and negative predictive values depend on disease burden, these parameters may not be generalizable to regions with a different incidence of COVID19 infections and should be implemented with care in the decision-making processes. Also, there is growing discussion on the role of screening asymptomatic subjects without clinical suspicion of COVID19, for example before surgery. Therefore we explored the situation in the Netherlands through a survey, aiming to provide data on the performance of imaging tests across a range of disease prevalence and on the use of imaging in screening setting.

Methods

We performed a nationwide survey in 79 hospitals and asked chest radiologists to provide the data to calculate diagnostic accuracy of chest radiography (CXR) and/or computed tomography (CT) for patients suspected of COVID19. We asked for the number of examinations performed, number of examinations with normal results and number of examinations with results suspected of COVID19 in relation to RT-PCR confirmed COVID19 infection (PCR+COVID19) as the reference standard. We excluded numeric data from hospitals that provided data on less than 10 patients, or hospitals that performed CT after negative RT-PCR results in clinically suspected patients. We also collected data on asymptomatic individuals who underwent CT imaging screening to rule out COVID19 infection either before surgery or in the emergency department. We calculated sensitivity, specificity and predictive values for the different imaging modalities, and presented these in relation to the observed probability of PCR+COVID19.

Results

Of 79 hospitals (8 academic) a total of 38 hospitals (8 academic) participated in the survey (response rate 48%).

Twenty-eight hospitals used CT (74%) as imaging test in the work-up of patients with suspected COVID19 infection, of which 6/8 (75%) academic and 22/31 non-academic (71%). Data from three hospitals were excluded from further analysis (CT performed after negative PCR, N=2 and total cases <10, N=1). Therefore, nine hospitals provided diagnostic accuracy data for CT in 899 patients (Table 1). In these hospitals the pre-test probability of COVID19 ranged from 9% to 70%. The positive predictive value (probability for PCR+COVID19 after a positive CT) ranged from 37%-90%. The inverse of the negative predictive value (probability for PCR+COVID19 after a negative CT) ranged from 0%-27%. If one defines a post-test (positive) probability ≥80% as

sufficient to establish the diagnosis, four out of nine (44%) hospitals did not reach this target. If one defines a post-test (negative) probability ≤5% as sufficient to rule out the diagnosis, six out of nine (67%%) hospitals did not reach this target (Figure 1).

Thirty-one (82%) hospitals used CXR as imaging test as part of the COVID19 diagnostic work-up. Three hospitals provided diagnostic accuracy data for 460 patients (Table 2). In these hospitals the pre-test probability of PRC+COVID19 ranged from 32% to 84%. The positive predictive value (probability for PCR+COVID19 after a positive CXR) ranged from 63%-93%. The inverse of the negative predictive value (probability for PCR+COVID19 after a negative CXR) ranged from 16%-70%. When one defines a post-test (positive) probability ≥80% as sufficient to establish the diagnosis, one of the three (33%) hospitals did not reach this target. When a post-test (negative) probability ≤5% is judged to be sufficient to exclude the diagnosis, none (0%) of the hospitals reached this target (Figure 2).

None of the radiology departments used ultrasound for diagnosis or follow-up of COVID-19 pneumonia.

Twenty-two hospitals (58%) reported to perform screening CT in asymptomatic subjects at the emergency department or in pre-operative setting. Eight hospitals provided frequency statistics on screening CT (two hospitals were excluded because of <10 patients and one was excluded because the CT indication was based on clinical indication). In the five remaining hospitals a total of 288 subjects were scanned with a yield of seven (2%) cases with some level of suspicion of COVID19 infection. In three patients (1%) this resulted in altered treatment strategy such as postponement of surgery, though one of these patients did have symptoms in retrospect.

Discussion

The first diagnosis of COVID19 in the Netherlands was confirmed on February 27, 2020. On April 1st the number of registered cases in the Netherlands was 14,829. The current survey was open March 30th – April 1st 2020 and therefore captured data on the first period of the pandemic in the Netherlands.

The data show that in patients with suspected COVID19 disease the performance of both CXR and CT to 'diagnose' a RT-PCR positive COVID19 diagnosis was modest to good, and somewhat dependent on the disease prevalence. Excluding the diagnosis using CXR was not possible, whereas CT could be used in a third of the hospitals to exclude RT-PCR positive COVID19 diagnosis (defined as a post-test probability <5%). This however seems to become more difficult

with higher disease prevalence. Data on CT performance in screening setting (asymptomatic patients without COVID19 suspicion) are limited. In these preliminary results we identified changes in management in a few of patients, but whether these changes were of benefit to the patient are uncertain. We propose, as from this moment, to at least prospectively register the use and impact of CT as screening tool in the hospitals that perform screening to determine whether there may be a role for CT, though randomized studies are required to proof benefits.

Multiple limitations of this initial survey need acknowledgement. First, survey data in general have significant, well-known limitations. Second, our definition of PCR+COVID19 needs to be addressed. A RT-PCR-based definition is by no means a gold standard, but in the current acute setting, this was the most practical, reliable approach. In the survey we did not control for differences between hospitals in the type of RT-PCR and whether one or multiple tests were done. Third, radiologists and hospitals will likely use different thresholds to define a CXR or CT as positive, which was not evaluated. Fourth, we arbitrarily used ≥80% certainty as a cut-off for 'diagnosis present' and ≤5% for 'diagnosis excluded' in patients with suspected COVID19 based on clinical presentation. In screening setting choosing a 5% cut-off value might be too high for excluding the diagnosis. Finally, acquiring images in COVID19 (suspected) patients may not only be for diagnostic purposes, but also for providing an estimation of severity of pulmonary involvement and patient prognosis. One could argue that CT is preferred over CXR for this purpose as it allows for more detailed disease burden assessment. On the other hand, readily available CXR is able to depict the more severe cases and to identify the clinically relevant group swiftly.

In conclusion, multiple imaging strategies can aid the diagnosis, exclusion and management of COVID19 patients. Such strategies depend on regional disease burden, availability of PCR, hospital setting and local preferences.

Table 1. Diagnostic performance of CT for PCR+ COVID-19 in relation to disease probability

Survey estimated prevalence	N, tot	PPV	NPV	Sens	Spec	FP rate	FN rate	Accuracy	Pre-test prob	LR+	LR-	Post-test Pos prob	Pos-test Neg prob
High	223	0.61	0.93	0.90	0.69	0.31	0.10	0.76	0.35	2.88	0.15	0.74	0.13
High	141	0.86	0.73	0.90	0.64	0.36	0.10	0.82	0.70	2.52	0.16	0.72	0.14
Intermediate	35	0.37	1.00	1.00	0.57	0.43	0.00	0.66	0.20	2.33	0.00	0.70	0.00
Intermediate	257	0.90	0.99	0.92	0.98	0.02	0.08	0.97	0.15	50.43	0.08	0.98	0.07
Intermediate	15	0.60	0.90	0.75	0.82	0.18	0.25	0.80	0.27	4.13	0.31	0.80	0.23
Intermediate	125	0.63	0.98	0.98	0.64	0.36	0.02	0.77	0.38	2.69	0.03	0.73	0.03
Low	13	0.86	0.83	0.86	0.83	0.17	0.14	0.85	0.54	5.14	0.17	0.84	0.15
Low	22	0.40	1.00	1.00	0.85	0.15	0.00	0.86	0.09	6.67	0.00	0.87	0.00
Unkown	68	0.86	0.95	0.92	0.90	0.10	0.08	0.91	0.38	9.69	0.09	0.91	0.08

Table 2. Diagnostic performance of chest radiography for PCR+ COVID-19 in relation to disease probability

Survey estimated prevalence	N, tot	PPV	NPV	Sens	Spec	FP rate	FN rate	Accuracy	Pre-test prob	LR+	LR-	Post-test Pos prob	Pos-test Neg prob
High	362	0.93	0.30	0.67	0.72	0.28	0.33	0.68	0.84	2.44	0.45	0.71	0.31
Intermediate	41	0.86	0.62	0.83	0.67	0.33	0.17	0.78	0.71	2.48	0.26	0.71	0.21
Low	57	0.63	0.84	0.67	0.82	0.18	0.33	0.77	0.32	3.71	0.41	0.79	0.29

Table 3. Screening CT in asymptomatic persons without clinical suspicion of COVID-19

Survey estimated prevalence	Screening indication	CT total	CT Negative	CT Positive	Management change
High	Surgery	99	96 (97%)	3	0
Intermediate	Surgery	15	15 (100%)	0	0
Intermediate	ED and surgery	73	71 (97%)	2	2
Intermediate	ED and surgery	37	36 (97%)	1	0
Intermediate	ED and surgery	64	63 (98%)	1^	1

^ In retrospect the patient did have symptoms

ED= Emergency department

Figure 1. Diagnostic performance of CT for PCR+ COVID-19 in relation to disease probability

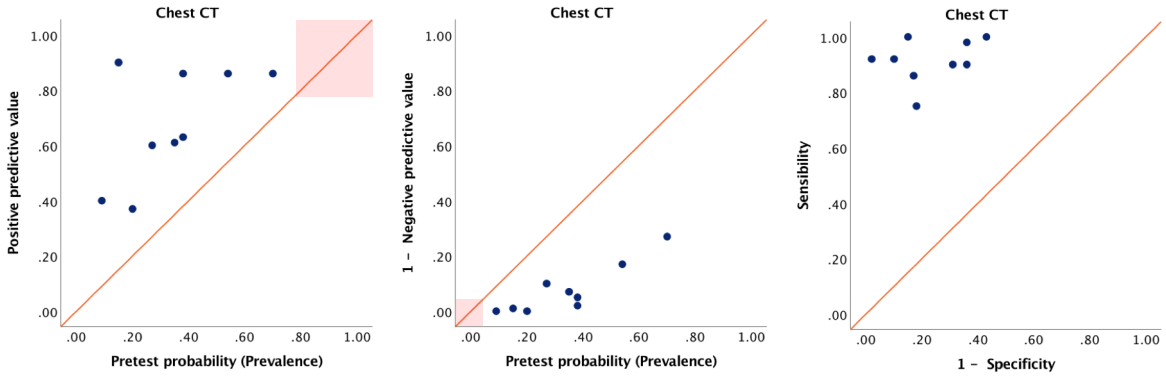

Figure 2. Diagnostic performance of chest radiography for PCR+ COVID-19 in relation to disease probability