

Evaluation of a comprehensive pre-procedural screening protocol for COVID-19 in times of a high SARS CoV-2 prevalence: a prospective cross-sectional study

Björn Stessel^{a,b,*}, Ina Callebaut^{a,b,*}, Frédéric Polus^a, Laurien Geebelen^a, Stefan Evers^a, Jean-Paul Ory^a, Koen Magerman^{b,c}, Geert Souverijns^d, Geert Braeken^a, Dirk Ramaekers^{e,f} and Janneke Cox^{b,g}

^aDepartment of Intensive Care and Anaesthesiology, Jessa Hospital, Hasselt, Belgium; ^bUHasselt, Faculty of Medicine and Life Sciences, LCRC, Diepenbeek, Belgium; ^cClinical Laboratory, Jessa Hospital, Hasselt, Belgium; ^dDepartment of Radiology, Jessa Hospital, Hasselt, Belgium; ^eJessa Hospital, Hasselt, Belgium; ^fLeuven Institute for Healthcare Policy (LIHP), University of Leuven, Leuven, Belgium; ^gDepartment of Infectious Diseases and Immunity, Jessa Hospital, Hasselt, Belgium

ABSTRACT

Background: To minimise the risk of COVID-19 transmission, an ambulant screening protocol for COVID-19 in patients before admission to the hospital was implemented, combining the SARS CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) on a nasopharyngeal swab, a chest computed tomography (CT) and assessment of clinical symptoms. The aim of this study was to evaluate the diagnostic yield and the proportionality of this pre-procedural screening protocol.

Methods: In this mono-centre, prospective, cross-sectional study, all patients admitted to the hospital between 22nd April 2020 until 14th May 2020 for semi-urgent surgery, haematological or oncological treatment, or electrophysiological investigation underwent a COVID-19 screening 2 days before their procedure. At a 2-week follow-up, the presence of clinical symptoms was evaluated by telephone as a post-hoc evaluation of the screening approach. Combined positive RT-PCR assay and/or positive chest CT was used as gold standard. Post-procedural outcomes of all patients diagnosed positive for COVID-19 were assessed.

Results: In total, 528 patients were included of which 20 (3.8%) were diagnosed as COVID-19 positive and 508 (96.2%) as COVID-19 negative. 11 (55.0%) of COVID-19 positive patients had only a positive RT-PCR assay, 3 (15.0%) had only a positive chest CT and 6 (30%) had both a positive RT-PCR assay and chest CT. 10 out of 20 (50.0%) COVID-19 positive patients reported no single clinical symptom at the screening. At 2 week follow-up, 50% of these patients were still asymptomatic. 37.5% of all COVID-19 negative patients were symptomatic at screening. In the COVID-19 negative group without symptoms at screening, 78 (29.3%) patients developed clinical symptoms at a 2-week follow-up.

Conclusion: This study suggests that routine chest CT and assessment of self-reported symptoms have limited value in the pre-procedural COVID-19 screening due to low sensitivity and/or specificity.

ARTICLE HISTORY

Received 24 September 2020
Accepted 13 January 2021



KEYWORDS

COVID-19; ambulant screening; screening protocol


Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the ongoing pandemic of coronavirus disease 2019 (COVID-19). This coronavirus was first detected in China in December 2019. Worldwide, the number of new COVID-19 cases and deaths continued to rise with 79 million cumulative and 1.7 million deaths globally since the start of the pandemic, as stated by the World Health Organisation (WHO) on 28th December 2020 [1]. The

disease severity can vary from asymptomatic carriers to pneumonia and death [2]. Belgium has reported 638 877 COVID infections so far, with a death rate of 3.0% [3]. During the first wave of COVID-19 infections, the Jessa hospital was located in the centre of the national epidemic. According to local regulations, all non-urgent elective surgeries, consultations, and therapies were halted according from 14th March 2020 till 10th May 2020. However, semi-urgent surgery, haematological and oncological therapies, and investigations

CONTACT Björn Stessel  bjorn.stessel@jessazh.be  Department of Intensive Care and Anesthesiology, Jessa Hospital – Hasselt, Virga-Jesse Campus, Stadsomvaart 11, Hasselt 3500, Belgium

*Joint first author.

 Supplemental data for this article can be accessed [here](#).

© 2021 Jessa ziekenhuis vzw. Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

and electrophysiological procedures still had to be performed in the hospital.

One of the major concerns in managing these semi-urgent admissions was the prevention of in-hospital transmission of SARS CoV-2, both patient-patient and patient-health-care worker. In a case series of hospitalised patients with confirmed COVID-19 pneumonia in Wuhan, China, the human-to-human hospital-associated transmission of COVID-19 was suspected in 41% of patients [4]. In Italy, the infection rate of health care workers grew exponentially during the pandemic, and the prevalence of infection among health care workers exceeded 10% [5]. The risk of COVID-19 hospital-associated transmission not only endangers the health of hospitalised patients (who may be already weakened by their underlying medical conditions) and healthcare providers but may also lead to further loss of working force. As transmission from asymptomatic or pre-symptomatic carriers or people with mild or atypical symptoms has been documented [6] and universal screening for SARS-CoV-2 in patients admitted to hospital revealed a high percentage of asymptomatic infections [7,8], screening on the basis of symptoms only seemed unwise.

Therefore, screening patients before admission was deemed necessary to minimise the risk of hospital-associated SARS-CoV-2 transmission. An ambulant screening protocol for COVID-19 in all patients before semi-urgent admission to the hospital was implemented in the Jessa Hospital, Hasselt, Belgium. The gold standard for screening is the SARS CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) on the nasopharyngeal swab [9]. However, the sensitivity of this RT-PCR is reported between 63% and 78% [10–12]. To trace potentially false-negative patients, we supplemented this screening tool with a chest computed tomography (CT) and assessment of self-reported clinical symptoms associated with COVID-19.

The main objective of this study was to evaluate the diagnostic yield and the proportionality of this pre-procedural screening approach for COVID-19. The results of this study may provide valuable information for the development of guidelines and recommendations for COVID-19 pre-admission testing.

Methods

This mono-centre, prospective, observational, cross-sectional study was performed at the Jessa hospital, Hasselt Belgium, a 980-beds tertiary referral hospital. Results are reported according to the STrengthening the Reporting of OBservational studies in Epidemiology

(STROBE) statement [13]. This study is approved by the ethical committee of Jessa Hospital on 21st April 2020 and registered on clinicaltrials.gov (NCT04334252).

All adult patients scheduled for semi-urgent surgery, haematological or oncological treatment or electrophysiological investigation were eligible for study participation. Exclusion criteria were: 1. patients <18 years old, 2. inability to express themselves, or 3. an insufficient understanding of the Dutch language. Written informed consent was obtained from all participants.

Testing protocol

Screening of all patients for COVID-19 at the ambulant pre-procedural consultation facility in the Jessa Hospital 2 days before the planned semi-urgent procedure or therapy was instituted on April 13th. The screening included three different screening instruments. First, nasopharyngeal swabs were analysed with an in-house developed reverse-transcriptase PCR for the E-gene on the ARIES analyser (Luminex Corporation) in accordance with the World Health Organisation (WHO) protocol [9]. Second, a chest CT was performed to investigate four different radiologic signs suspect for COVID-19: 1. the presence of a crazy-paving pattern (yes or no), 2. the presence of ground-glass opacity (GGO) (yes or no, if yes: peripheral GGO and/or central GGO yes or no), 3. consolidation (yes or no), and 4. the number of infected lobes was assessed. In addition, the presence of pleura fluid enlarged lymph nodes, and masses in the lungs was also evaluated. Third, patients were asked to complete a baseline questionnaire to assess baseline characteristics including gender, age, BMI, smoking behaviour, living area, current working situation, highest degree, medical history, use of medication, the presence of house-mates with similar symptoms, and possible contact with confirmed COVID-19 positives together with the presence of clinical symptoms associated with COVID-19 at the date of screening. These symptoms were fever, myalgia, cough, sputum production, sore throat, anorexia, dyspnoea, rhinorrhoea, headache, anosmia, vomiting, and diarrhoea.

Post hoc evaluation of this screening method consisted of an assessment of the development of the same clinical symptoms associated with COVID-19 by telephone follow-up two weeks after the screening date.

Patients who were diagnosed positive for COVID-19 with either RT-PCR assay of the nasopharyngeal swab or CT thorax, were classified into either symptomatic or asymptomatic at baseline based on their pre-procedural symptoms, and the relationship between

preoperative and postoperative symptoms was assessed. Patients were classified as symptomatic if they reported presence of at least one symptom. Furthermore, post-procedural outcomes of all patients diagnosed positive for COVID-19 were assessed.

The primary endpoints of this study were the prevalence of laboratory confirmation of the RT-PCR assay of the nasopharyngeal swab, the prevalence of a positive chest CT, and the prevalence of clinical symptoms associated with COVID-19 at the date of screening. The secondary end point was the predictive value of clinical symptoms, a positive nasopharyngeal swab, and a positive CT thorax at the date of screening for the development of typical COVID-19 symptoms at follow-up, two weeks later.

Statistical analysis

Continuous data are shown as mean \pm standard deviation (SD) and categorical data are presented as frequencies (%). Analyses were performed with the Student's t-test for continuous data and Pearson's χ^2 or Fisher's exact test (in case of an observed count <10) for categorical data. A p-value of $p \leq .05$ was

considered statistically significant. All analyses were performed with SPSS 24.0 (IBM® SPSS® Inc, Chicago, Illinois, USA). Using the combination of laboratory confirmation of the RT-PCR assay of the nasopharyngeal swab and/or a positive chest CT as a gold standard, sensitivity and specificity, as well as positive and negative predictive values were calculated for the presence of typical COVID-19 symptoms at baseline, a positive chest CT and a positive RT-PCR assay of the nasopharyngeal swab.

Results

During the study period from 22nd April 2020 until 14th May 2020, 884 patients were invited to participate at the ambulant pre-procedural COVID-19 screening facility. In total, 528 patients were included in the study of which 20 patients were diagnosed as COVID-19 positive (3.79%) and 508 patients as COVID-19 negative (96.21%). A STROBE flowchart depicting inclusion and exclusion is shown in Figure 1.

Baseline patient's characteristics, including socio-economic status, are shown in Table 1, stratified per

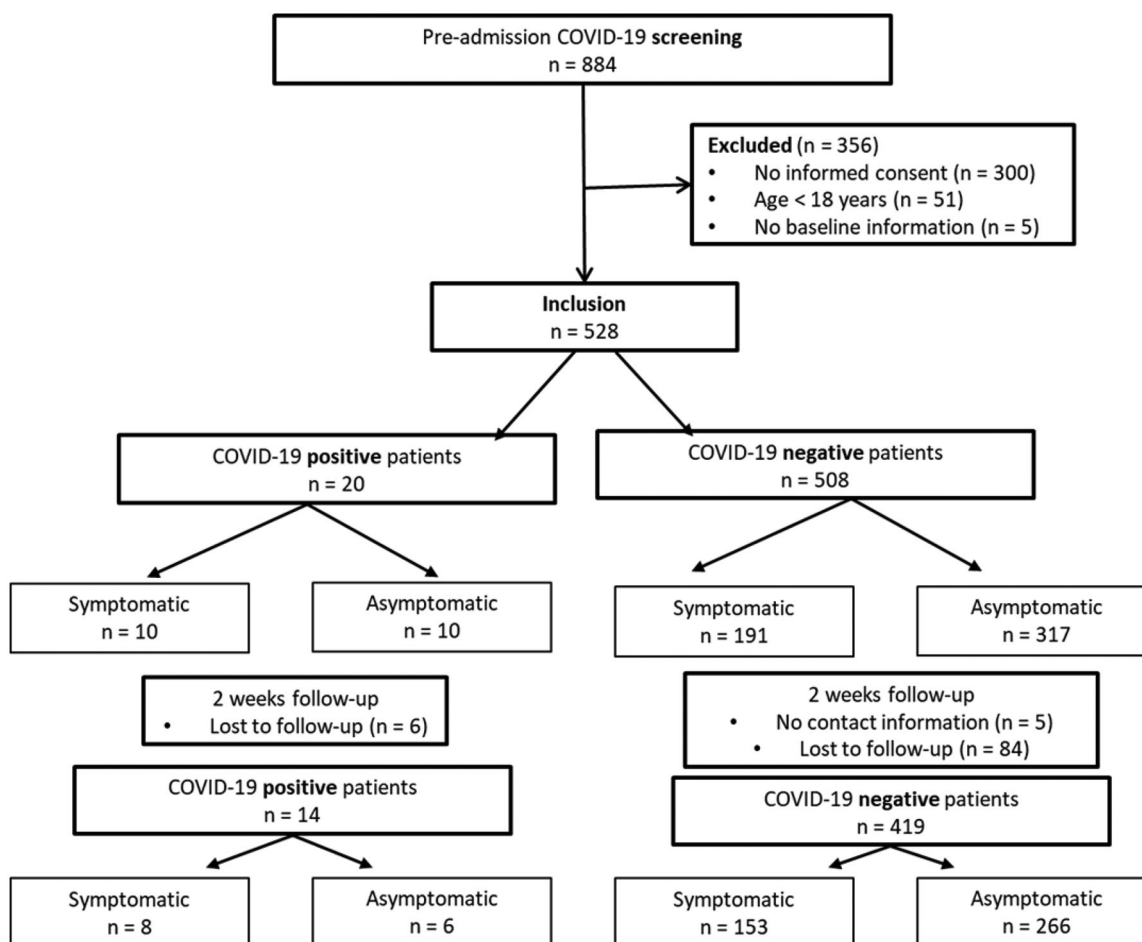


Figure 1. STROBE flowchart depicting inclusion and exclusion of study patients.

Table 1. Baseline patients characteristics stratified per group based on COVID-19 diagnosis.

Variable	COVID-19 negative patients <i>n</i> = 508	COVID-19 positive patients <i>n</i> = 20	<i>p</i> -Value
Age (years)	58.0 ± 16.7	61.4 ± 14.8	.39
Gender (male), <i>n</i> (%)	276 (54.3%)	15 (75.0%)	.14
BMI (kg/m ²) (<i>n</i> = 434)	26.0 ± 4.5	27.6 ± 5.1	.37
Length (m)	1.7 ± 0.1	1.7 ± 0.1	
Weight (kg)	76.8 ± 15.4	85.3 ± 22.1	
Smoking behaviour (<i>n</i> = 434)	<i>n</i> = 419	<i>n</i> = 14	.73
Yes, <i>n</i> (%)	69 (16.5%)	1 (7.1%)	
No, <i>n</i> (%)	344 (82.1%)	13 (92.9%)	
Stopped, <i>n</i> (%)	6 (1.4%)	0 (0.0%)	
Living area (<i>n</i> = 434)	<i>n</i> = 419	<i>n</i> = 14	.46
Hasselt, <i>n</i> (%)	85 (20.3%)	3 (21.4%)	
Neighbouring areas of Hasselt, <i>n</i> (%)	128 (30.5%)	4 (28.6%)	
Rest of Limburg, <i>n</i> (%)	176 (42.0%)	6 (42.9%)	
Rest of Belgium, <i>n</i> (%)	29 (6.9%)	0 (0.0%)	
Outside of Belgium, <i>n</i> (%)	1 (0.3%)	1 (7.1%)	
Current working situation (<i>n</i> = 434)	<i>n</i> = 419	<i>n</i> = 14	.69
Paid job, <i>n</i> (%)	104 (24.8%)	5 (35.7%)	
Self-employed, <i>n</i> (%)	14 (3.3%)	1 (7.1%)	
Charity/unpaid job, <i>n</i> (%)	3 (0.7%)	0 (0.0%)	
Unemployed, <i>n</i> (%)	27 (6.4%)	1 (7.1%)	
Incapacitated > 6 months, <i>n</i> (%)	55 (13.1%)	2 (14.4%)	
Retired, <i>n</i> (%)	209 (50.0%)	5 (35.7%)	
Student, <i>n</i> (%)	7 (1.7%)	0 (0.0%)	
Highest diploma obtained (<i>n</i> = 434)	<i>n</i> = 419	<i>n</i> = 14	.63
None, <i>n</i> (%)	13 (3.1%)	0 (0.0%)	
Primary school, <i>n</i> (%)	41 (9.8%)	0 (0.0%)	
Middle school, <i>n</i> (%)	234 (55.8%)	11 (78.6%)	
Graduate school, <i>n</i> (%)	84 (20.0%)	2 (14.3%)	
University, <i>n</i> (%)	45 (10.7%)	1 (7.1%)	
Doctorate or post-doctorate, <i>n</i> (%)	2 (0.6%)	0 (0.0%)	
Medical history			.78
Yes, <i>n</i> (%)	364 (71.7%)	15 (75.0%)	
No, <i>n</i> (%)	144 (28.3%)	5 (25.0%)	
Medication usage			.88
None, <i>n</i> (%)	228 (44.9%)	9 (45.0%)	
1 – 5, <i>n</i> (%)	142 (28.0%)	6 (30.0%)	
6 – 10, <i>n</i> (%)	111 (21.8%)	4 (20.0%)	
More than 10, <i>n</i> (%)	27 (5.3%)	1 (5.0%)	
House mates with similar symptoms, <i>n</i> (%)	17 (3.3%)	0 (0.0%)	.44
Contact with confirmed Covid-19 positives, <i>n</i> (%)	8 (1.6%)	2 (10.0%)	.03

Data are presented as numbers (%). A *p*-value <.05 is considered statistically significant (shown in bold).

group based on COVID-19 diagnosis. The mean (SD) age of all patients was 58.10 (16.58), 291 (55.11%) were male. Baseline analyses revealed that only recent contact with confirmed Covid-19 patients was significantly more frequent (*p* = .03) in the COVID-19 positive group.

The majority of COVID-19 positive patients (*n* = 11, 55.0%) had only a positive RT-PCR assay, six patients (30.0%) had both a positive RT-PCR assay and a positive chest CT, and another 3 patients (15.0%) had only a positive chest CT (Table 2). In all COVID-19 positive images, ground-glass opacities were present. These findings were associated with lung consolidations in 2 patients, while none of the positive CT images showed a crazy-paving pattern. The number of infected lobes varied among the patients (1 infected lobe (*n* = 1, 11.1%), 2 infected lobes (*n* = 2, 22.2%), 3 infected lobes (*n* = 1, 11.1%), 4 infected lobes (*n* = 1, 11.1%) and 5 infected lobes (*n* = 4, 44.5%). The presence of pleura fluid was seen in 1 patient.

Due to the regulations at the time of the study, 10 semi-urgent procedures and/or surgeries were postponed to a later time point in confirmed COVID-19 patients. One adult accompanying her child to the hospital for a semi-urgent procedure was found positive, resulting in 9 procedures and/or surgeries that were conducted in COVID-19 positive patients and of which 4 procedures were conducted in an ambulatory setting, resulting in a median (interquartile range) length-of-stay of 1 (0, 5) day. No postoperative complications occurred in these patients. One COVID-19 positive patient with an extensive oncological history died within 2 weeks after his ambulant procedure, however, the cause of death was stated a natural non-COVID related death.

In total, 201 (38.1%) of all study patients reported one or more clinical symptoms of COVID-19 at screening (Table 2A). No significant difference in self-reported clinical symptoms was seen between COVID-19 positive and negative patients both at baseline

Table 2. Frequency tables of all study patients.

A		
Screening	Symptoms at baseline	No symptoms at baseline
Total patient group (<i>n</i> = 528)	201 (38.1%)	327 (61.9%)
COVID-19 negative patients (<i>n</i> = 508)	191 (37.6%)	317 (62.4%)
COVID-19 positive patients (<i>n</i> = 20)	10 (50.0%)	10 (50.0%)
B		
Total patient group (<i>n</i> = 433)	Symptoms at follow-up (<i>n</i> = 176)	No symptoms at follow-up (<i>n</i> = 257)
Symptoms at screening (<i>n</i> = 161) (37.2%)	103 (64.0%)	58 (36.0%)
No symptoms at screening (<i>n</i> = 272) (62.8%)	73 (26.8%)	199 (73.2%)
C		
Covid-19 positives (<i>n</i> = 14)	Symptoms at follow-up (<i>n</i> = 7)	No symptoms at follow-up (<i>n</i> = 7)
Symptoms at screening (<i>n</i> = 8) (57.1%)	4 (50.0%)	4 (50.0%)
No symptoms at screening (<i>n</i> = 6) (42.9%)	3 (50.0%)	3 (50.0%)
D		
Covid-19 negatives (<i>n</i> = 419)	Symptoms at follow-up (<i>n</i> = 169)	No symptoms at follow-up (<i>n</i> = 250)
Symptoms at screening (<i>n</i> = 153) (36.5%)	91 (59.5%)	62 (40.5%)
No symptoms at screening (<i>n</i> = 266) (63.5%)	78 (29.3%)	188 (70.1%)
E		
Covid-19 negatives without malignancies (<i>n</i> = 364)	Symptoms at follow-up (<i>n</i> = 134)	No symptoms at follow-up (<i>n</i> = 230)
Symptoms at screening (<i>n</i> = 124) (34.1%)	71 (57.3%)	53 (42.7%)
No symptoms at screening (<i>n</i> = 240) (65.9%)	63 (26.3%)	177 (73.7%)

(A) Total patient groups at screening (B) Total patient group with a follow-up moment (C) Covid-19 positive patients with a follow-up moment (D) Covid-19 patients with a follow-up moment and COVID-19 negative patients without malignancies (E). The patients are stratified based on reporting of any clinical symptom at screening and at follow-up. Data are presented as numbers (%).

(50% vs 37.6%, $p = .26$) and follow-up (50% vs 40.3%, $p = .47$). Overall, 73 (26.8%) of patients without any clinical symptom of COVID-19 at screening, developed one or more clinical symptoms of COVID-19 at two-week follow-up (Table 2B). In the COVID-19 negative group without symptoms at screening, 78 (29.3%) patients developed clinical symptoms at a 2-week follow-up (Table 2D). After the exclusion of patients with malignancies (these patients are prone to developing various symptoms due to underlying disease), still, 63 (26.3%) asymptomatic patients at screening were symptomatic at follow-up (Table 2E).

Based on these results, we calculated sensitivity, specificity, and predictive values of the three different preoperative screening measures (Table 3).

An overview of individual clinical symptoms reported by patients at screening and 2-week follow-up, stratified per group based on COVID-19 diagnosis, is presented in Table 4. At baseline, anorexia ($p = .01$) and anosmia ($p = .04$) were statistically significantly more reported by patients with confirmed COVID-19 diagnosis at screening (Table 4). At 2 weeks follow-up, only headache ($p = .007$), was statistically significantly more reported by patients with prior confirmed COVID-19 diagnosis.

Sixty of the included patients had a cancer diagnosis. Of these 58 were COVID-19 negative. When

comparing the COVID negative patients with and without malignancy we found significantly more myalgia and anorexia in the malignancy group (Supplementary Table 1A+B). This discrepancy is most likely to be associated with the diagnosed malignancy and corresponding therapy.

Discussion

In this mono-centre, prospective, cross-sectional study, when screening all patients scheduled for (semi)-urgent in-hospital procedures, 3.79% of all the enrolled patients were diagnosed with COVID-19. The RT-PCR assay of the nasopharyngeal swabs diagnosed most COVID-19 patients (85%). A positive chest CT was found in 45% of patients, however, of these 30% was also diagnosed with RT-PCR. Clinical symptoms were as frequent in COVID-19 positive patients as in COVID-19 negative patients.

These results are in line with recent literature. The prevalence of SARS-CoV-2 infection identified on pre-procedural surveillance in a cohort of 11,540 patients was also low in another study, with a peak rate of 4.3% that fell below 0.3% after April 2020 [14]. The relatively low prevalence of COVID-19 infection (3.8%) in this cohort is at the same level of prevalence of immunity for COVID-19 observed in the Belgian

Table 3. Sensitivity, specificity, and predictive values of individual preoperative screening measures.

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Positive RT-PCR assay	85.0% (62.1% to 96.7%)	100% (99.3% to 100%)	100.0%	99.4% (98.4% to 99.8%)
Positive Chest CT	45.0% (23.1% to 68.5%)	100% (99.3% to 100%)	100.0%	97.9% (96.9% to 98.6%)
Symptoms	50.0% (27.2% to 72.8%)	62.4% (58.0% to 66.6%)	5.0% (3.2% to 7.6%)	96.9% (95.3% to 98.0%)

The 95% confidence intervals are presented in parentheses.

Table 4. Overview of clinical symptoms reported by patients at screening and at 2 week follow-up, stratified per group based on COVID-19 diagnosis.

At screening	COVID-19 negative patients <i>n</i> = 508	COVID-19 positive patients <i>n</i> = 20	<i>p</i> -Value
Fever (> 38 °C), <i>n</i> (%)	5 (1.0%)	0 (0.0%)	.66
Myalgia, <i>n</i> (%)	62 (12.2%)	2 (10.0%)	.83
Cough, <i>n</i> (%)	32 (6.3%)	1 (5.0%)	.85
Sputum production, <i>n</i> (%)	19 (3.7%)	0 (0.0%)	.39
Pharyngalgia, <i>n</i> (%)	19 (3.7%)	2 (10.0%)	.14
Anorexia, <i>n</i> (%)	20 (3.9%)	3 (15.0%)	.01
Dyspnoea, <i>n</i> (%)	58 (11.4%)	2 (10.0%)	.91
Runny nose, <i>n</i> (%)	50 (9.8%)	1 (5.0%)	.51
Headache, <i>n</i> (%)	35 (6.9%)	1 (5.0%)	.78
Anosmia, <i>n</i> (%)	13 (2.6%)	2 (10.0%)	.04
Nausea/vomiting, <i>n</i> (%)	8 (1.6%)	0 (0.0%)	.58
Diarrhoea, <i>n</i> (%)	17 (3.3%)	1 (5.0%)	.65
2 weeks follow-up	COVID-19 negative patients <i>n</i> = 419	COVID-19 positive patients <i>n</i> = 14	<i>p</i> -Value
Fever (> 38 °C), <i>n</i> (%)	5 (1.2%)	0 (0.0%)	.72
Myalgia, <i>n</i> (%)	51 (12.2%)	1 (7.1%)	.69
Cough, <i>n</i> (%)	27 (6.4%)	0 (0.0%)	.70
Sputum production, <i>n</i> (%)	17 (4.1%)	0 (0.0%)	.35
Pharyngalgia, <i>n</i> (%)	18 (4.3%)	2 (14.3%)	.55
Anorexia, <i>n</i> (%)	14 (1.0%)	2 (14.3%)	.91
Dyspnoea, <i>n</i> (%)	49 (12.0%)	1 (7.1%)	.27
Runny nose, <i>n</i> (%)	39 (9.3%)	1 (7.1%)	.78
Headache, <i>n</i> (%)	25 (6.0%)	4 (28.5%)	.007
Anosmia, <i>n</i> (%)	11 (2.6%)	2 (14.3%)	.35
Nausea/vomiting, <i>n</i> (%)	5 (1.2%)	0 (0.0%)	.61
Diarrhoea, <i>n</i> (%)	11 (2.6%)	1 (7.1%)	.76

Data are presented as numbers (%). A *p*-value <.05 is considered statistically significant (shown in bold).

population: on 30th March only 2.1% of the population showed antibodies against COVID-19, while this rose to 4.1% on 14th April 2020 [3]. As we performed our study in patients that were scheduled for semi-urgent admission, we expect positivity to be similar to that of the general population.

The sensitivity of RT-PCR assays for diagnosis of COVID-19 can vary and is reported between 63% and 78% [10–12]. In this study, only 15% of patients with confirmed COVID-19 diagnosis had a negative RT-PCR result in the nasopharyngeal swab. This observed sensitivity of 85% for RT-PCR may however be an over-estimation due to the risk of missing patients with a combined negative RT-PCR and chest CT result. A low viral density in pre-symptomatic patients, lab errors, collection of inadequate nasopharyngeal material, or improper specimen transportation are identified as sources of false-negative testing [15]. Nasopharyngeal swabs may not be the most sensitive methods of screening asymptomatic patients. In addition, Zou *et al.* detected that viral loads in the nasal cavity were 64-fold higher compared to the pharynx [16], while

others detect higher positive rates in sputum samples [17] or bronchoalveolar lavage [11]. None of the included patients developed COVID-19 during the admission, however length-of-stay was rather short. We were unable to assess what proportion of patients that were screened negative, did receive a COVID-19 diagnosis afterwards.

Chest CTs have been proposed for the diagnosis of COVID-19, to increase sensitivity of testing when combined with RT-PCR [18]. In this study, 45% of the COVID-19 patients had abnormal CT findings, however, only 15% of COVID-19 positive patients were diagnosed exclusively by chest CT. Indeed, a systematic review concluded that 26 out of 55 included studies reported the presence of normal chest CT findings in COVID-19 positive patients [18]. High rates (up to 56%) of normal chest CT findings were reported in asymptomatic patients or with mild symptoms [18]. Furthermore, chest CT findings of COVID-19 infection are not pathognomonic as it lacks specificity in differentiating from other causes of pneumonia and have a high cost, both in terms of monetary as radiation

[18,19]. Therefore, our findings support the American College of Radiology recommendation, that CT scans should not be used to screen for or as a first-line test to diagnose COVID-19 and that CT scans should be used sparingly and reserved for hospitalised, symptomatic patients with specific clinical indications for CT [20].

We found no significant difference in the presence of one or more clinical symptoms at screening between COVID-19 negative and positive patients. Dyspnoea and runny nose were among the 3 most frequently reported symptoms in COVID-19 negative patients. A possible explanation for the high rate of symptomatic patients in the COVID-19 negative group may be found in the exposure of seasonal allergens such as birch pollen and grass pollen. These seasonal allergens were present during the study period, possibly causing a bias [21]. Moreover, the symptoms that were assessed clearly lack specificity for COVID-19, except for anorexia and anosmia, that were found more frequently in COVID-positive patients. A sub-analysis of patients with and without malignancies shows no large differences in symptoms at screening and at 2 weeks follow up."

Our observation that 50% of COVID-19 positive patients were asymptomatic at screening and that 50% of these asymptomatic patients were still asymptomatic at 2-week follow-up is in line with the literature. Kim *et al.* reported as much as one-fifth of a cohort of individuals with COVID-19 remaining asymptomatic [22] while literature indicates in various populations that asymptomatic or pre-symptomatic patients can test positive for SARS-CoV2 at rates ranging from 17.9% to 57% of those who test positive showing no symptoms [23]. In England, only 33% of all patients with a positive SARS CoV2 test between 26th April and 27th June 2020 reported symptoms [24]. In an obstetrical population in New York City, even 87.9% of COVID-19 positive patients were asymptomatic at admission and only 10% of these patients developed symptoms before postpartum discharge [8].

In this study, 29.3% of asymptomatic patients at the screening with a negative COVID-19 test developed one or more symptoms at two weeks follow-up. Theoretically, all these patients may have tested falsely negative on the COVID-19 test. However, it is more likely that they have developed symptoms elicited by their underlying disease, treatment, or seasonal allergy.

Besides pre-admission testing, it remains of the highest importance to reduce the risk of in-hospital transmission by the correct and universal application

of personal protective equipment (PPE). Indeed, the American Society of Anaesthesiologists (ASA)/Anesthesia Patient Safety Foundation (APSF) Statement on Perioperative Testing for the COVID-19 Virus not only recommends nucleic acid amplification testing (including PCR tests) in all patients prior to undergoing non-emergent surgery and postponement of elective procedures if a patient tests positive, but also that droplet precautions (surgical mask and eye covering) should be used by operation room staff for operative cases [25]. Before performing an aerosol-generating procedure, health care providers within the room should even wear an N95 mask, eye protection, gloves and a gown [25].

This study has some limitations. First, a fair amount of eligible patients were excluded because of missing informed consent. This can be attributed to the organisational difficulties the hospital was facing at that time to provide sufficient care for COVID-19 positive patients as well as providing (semi) urgent surgeries and therapies for all patients. Second, the evaluation of clinical symptoms was performed in an empirical way in this study where only the presence was evaluated. Further research should focus on the severity of the symptoms, potentially scored with a Numerical Rating Scale, together with the attribution of these symptoms to COVID-19. Third, due to the mono-centre design of this study and the relatively low numbers of inclusions, results cannot be generalised to the (Belgian) general population. Finally, we did not systematically performed repeated COVID-19 testing after 2 weeks, so the predictive value of the different diagnostic modalities including the clinical symptoms for the future development of COVID-19 could not be assessed.

In conclusion, the results of this study support the recommendation that RT-PCR should not be supplemented by chest CT in a first-line test protocol to screen for or diagnose COVID-19. This study also suggests that the assessment of self-reported symptoms only has limited value in the pre-procedural screening for COVID-19 due to low specificity and sensitivity. A waterproof pre-procedural screening protocol for COVID-19 seems at this time utopian and therefore universal application of personal protective equipment (PPE) in a hospital environment remains of utmost importance.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Data availability statement

Due to the applicable privacy regulation (GDPR) and Good Clinical Practices (GCP) legislation, the full underlying dataset supporting the study cannot be provided. This dataset contains potentially identifying information, for example age, BMI and data of admission to the hospital leading to a unique subject in the dataset. Therefore, descriptive statistics have been used for a general overview of our study population, and all other relevant information is provided in Table 1.

Anonymized data is available on motivated request and can be sent to: Prof. dr. BjörnStessel; Salvatorstraat 20; 3500 Hasselt, Belgium; bjorn.stessel@jessazh.be; AND Jessa Ziekenhuis, Data Protection Officer (DPO); Stadsomvaart 11; 3500 Hasselt, Belgium; DPO@jessazh.be.

References

- [1] World Health Organisation. 2020. [cited 2020 Dec 28]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
- [2] Lai CC, Liu YH, Wang CY, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): facts and myths. *J Microbiol Immunol Infect.* 2020;53(3):404–412.
- [3] Sciensano. Weekly reports Sciensano Belgium. Sciensano, 2020. Available from: www.sciensano.be.
- [4] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020;323(11):1061–1069.
- [5] Felice C, Di Tanna GL, Zanus G, et al. Impact of COVID-19 outbreak on healthcare workers in Italy: results from a National E-Survey. *J Community Health.* 2020;45(4):675–683.
- [6] Klompas M, Morris CA, Sinclair J, et al. Universal masking in hospitals in the Covid-19 era. *N Engl J Med.* 2020;382(21):e63.
- [7] Gruskay JA, Dvorzhinskiy A, Konnaris MA, et al. Universal testing for COVID-19 in essential orthopaedic surgery reveals a high percentage of asymptomatic infections. *J Bone Joint Surg Am.* 2020; 102(16):1379–1388.
- [8] Sutton D, Fuchs K, D'Alton M, et al. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med.* 2020;382(22):2163–2164.
- [9] WHO. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. Interim Guidance. :1–7.
- [10] Zitek T. The appropriate use of testing for COVID-19. *West J Emerg Med.* 2020;21(3):470–472.
- [11] Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA.* 2020; 323(18):1843–1844.
- [12] Katz A P, Civantos F J, Sargi Z, et al. False-positive reverse transcriptase polymerase chain reaction screening for SARS-CoV-2 in the setting of urgent head and neck surgery and otolaryngologic emergencies during the pandemic: Clinical implications. *Head & Neck.* 2020;42(7):1621–1628. doi:10.1002/hed.26317.
- [13] von Elm E, Altman DG, Egger M, STROBE Initiative, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Prev Med.* 2007;45(4):247–251.
- [14] Aslam A, Singh J, Robilotti E, et al. SARS CoV-2 surveillance and exposure in the perioperative setting with universal testing and Personal Protective Equipment (PPE) policies. *Clin Infect Dis.* 2020; ciae1607.
- [15] Vinh DB, Zhao X, Kiong KL, et al. Overview of COVID-19 testing and implications for otolaryngologists. *Head Neck.* 2020;42(7):1629–1633.
- [16] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med.* 2020;382(12):1177–1179.
- [17] Yang YY, Shen C, et al. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infection med rxiv. The Innovation, 2020. Available from: <https://www.medrxiv.org/content/101101/2020021120021493v2/fullpdf+html>.
- [18] Sun Z, Zhang N, Li Y, et al. A systematic review of chest imaging findings in COVID-19. *Quant Imaging Med Surg.* 2020;10(5):1058–1079.
- [19] Xu B, Xing Y, Peng J, et al. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. *Eur Radiol.* 2020;30(10): 5720–5727. doi:10.1007/s00330-020-06934-2.
- [20] Radiology ACo. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. [cited 2020 Mar 11]. Available from: www.acr.org/2020.
- [21] Belgium: Sciensano; Newsletter 2020, AirAllergy.be; 2020. Available from: www.airallergy.be.
- [22] Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. *Clin Microbiol Infect.* 2020;26(7):948.e1–e3.
- [23] Lee S, Meyler P, Mozel M, et al. Asymptomatic carriage and transmission of SARS-CoV-2: What do we know?. *Can J Anesth/j Can Anesth.* 2020;67(10): 1424–1430. doi:10.1007/s12630-020-01729-x.
- [24] Statistics OfN. Coronavirus (COVID-19) infection in the community in England: July 2020. [cited 2020 Jul 07]. Available from: <https://www.ons.gov.uk/>.
- [25] Foundation ASoAaAPS. ASA/APS statement on perioperative testing for the COVID-19 virus. 2020. [cited 2020 Jun 3]. Available from: <https://www.asahq.org/about-asa/newsroom/news-releases/2020/04/asa-and-apsf-joint-statement-on-perioperative-testing-for-the-covid-19-virus>.