Clinical characteristics, multi-organ dysfunction, and outcomes of patients with COVID-19: A prospective observational study

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Abstract:	**Background** Characterizing the multi-organ manifestations and outcomes of patients hospitalized with COVID-19 will inform resource requirements to address the long-term burden of this disease. We sought to characterize the clinical trajectory of organ dysfunction, management of disease sequelae, and short- and long-term outcomes of hospitalized patients with COVID-19. **Methods**

We conducted a prospective observational study of adult patients with COVID-19 admitted to one of two hospitals in London, Canada during the first wave of the pandemic. We recorded patients' baseline characteristics, physiological parameters, measures of organ function, and therapies administered during hospitalization in non-ICU and ICU patients, and compared the characteristics of hospital survivors to non-survivors. Finally, we recorded follow-up thoracic computerized tomography (CT) and echocardiographic findings after hospital discharge.

Results

We enrolled 100 consecutive patients (53 women) hospitalized with COVID-19, including 32 patients who received ICU care and 68 who were treated in non-ICU settings. Respiratory sequelae were common: 23% received high flow oxygen by nasal cannula, 9% received non-invasive ventilation, 24% received invasive mechanical ventilation, and 2% received veno-venous extracorporeal membrane oxygenation. Overall, 9% of patients had cerebrovascular events (4% ischemic stroke, 6% intracranial hemorrhage) and 6% had pulmonary embolism. After discharge, 11 of 19 patients had persistent abnormalities on CT thorax and 6 of 15 had persistent cardiac dysfunction on echocardiography.

Interpretation

COVID-19 is a multi-system disease involving neurological, cardiac, and thrombotic dysfunction, without evidence of hepatic dysfunction. Patients have persistent organ dysfunction after hospital discharge, underscoring the need for research on long-term outcomes of COVID-19 survivors.

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ABSTRACT

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INTRODUCTION

The typical clinical spectrum of Coronavirus disease 2019 (COVID-19), the illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), ranges from mild respiratory symptoms to multi-organ failure and death.[1, 2] Emerging evidence has shown that COVID-19 is associated with a range of pulmonary and extra-pulmonary organ involvement.[3] Although early Canadian data shed light on the outcomes and mortality rate, data on the morbidity of hospitalized patients has been sparse and often based on retrospectively collected databases,[4-6] and many have excluded patients hospitalized outside the ICU setting.[5-7]

To characterize COVID-19's clinical course, multi-organ involvement and outcomes, prospectively collected data are required. Such data will be well suited to inform Canadian healthcare priorities as they relate to both the long-term burden of COVID-19 and future pandemics. The objectives of this study are to describe the baseline characteristics, clinical presentation, spectrum of organ dysfunction, management of disease sequelae, and clinical outcomes of hospitalized patients with COVID-19.

METHODS

Study Design & Setting

This prospective observational study was conducted at two sites in London Health Sciences Centre (LHSC), a 1116-bed academic, tertiary care centre in London, Canada

that is comprised of two hospitals: Victoria Hospital and University Hospital. The study complied with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies.[8]

Patient Recruitment and Data Collection

We consecutively enrolled all adult patients (greater than 18 years of age) admitted to hospital with a diagnosis of COVID-19 (confirmed by a positive PCR assay) from March 17, 2020 until June 18, 2020.

We collected data from patients and their clinical team(s), paper charts, electronic medical records, and Critical Care Information System database. We recorded patients' baseline demographic characteristics, physiological parameters, investigations, and therapies administered throughout hospitalization in non-intensive-care unit (non-ICU) and ICU settings, and overall outcome (i.e., in-hospital death versus discharge from hospital and discharge destination). Finally, we recorded any echocardiography and thoracic computed tomography (CT; performed for clinical indications) results up until December 31, 2020 (Supplementary Material Online 1).

Statistical Analysis

We used descriptive statistics (means and standard deviations, medians and interquartile ranges [IQRs], and proportions and percentages, as appropriate) to summarize patients' baseline characteristics, physiological parameters, therapies, and outcomes.

We applied the Student's t-test, Wilcoxon rank-sum test, or chi-squared statistic, as appropriate, to compare characteristics of hospital survivors to non-survivors. In addition, we compared the characteristics of patients who were initially admitted to the ICU with patients who were admitted to a non-ICU location but were transferred to ICU due to clinical deterioration. We selected predictor variables based on prior retrospective data demonstrating an association between the variables and outcome of interest.[1, 9] They included age, vital signs at emergency department (ED) triage, laboratory data obtained on admission such as blood pH, white blood cell count, hemoglobin, platelets, lymphocyte count, lactate, ferritin, lactate dehydrogenase (LDH), c-reactive protein (CRP), and troponin levels. All statistical tests are two-sided with the threshold of statistical significance set at a p-value of less than 0.05. We performed all data analyses using Statistical Package for Social Sciences (SPSS) version 25.0 (IBM, Armonk, N.Y.).

Ethics Approval

Western University's Research Ethics Board approved the conduct of this study (Study number: 115732; date: April 1, 2020).

RESULTS

Baseline Characteristics

Between March 17th to June 18th, 2020, 101 patients were admitted to one of the participating hospitals with a positive for SARS-CoV-2 test. Of those, one patient declined to participate in the study. We included 100 patients (32 ICU and 68 non-ICU patients). An overview of the recruitment procedures is seen in figure 1. **Table 1** presents patients' baseline characteristics of patients.

Clinical Presentation

Table 2 presents patients' clinical characteristics at the time of hospital admission. Symptoms reported by more than 50% of patients at the time of hospitalization for COVID-19 were cough, dyspnea, fever, and fatigue. At the time of emergency department (ED) assessment, 44.2% (42/95) of patients presented with a respiratory rate (RR) > 20 breaths per minute) and 33/98 (33.7%) received supplemental oxygen therapy in the ED to maintain oxygen saturation levels above 92%.

Twenty patients were admitted to the ICU while 80 patients were admitted to the ward. Among the 80 patients initially admitted to the ward, 12 were eventually transferred to ICU after a median hospital stay of 0.5 days (IQR 0 to 2). Ultimately, 32 patients received ICU admission. An overview of the patient's clinical disposition while in hospital is shown in **Figure 1**.

Complications & Management by Organ System

Respiratory complications & therapies

Table 3 shows the respiratory complications and therapies received during hospitalization. Among all 100 patients, 79 (79%) received supplemental oxygen therapy including high flow nasal cannula (HFNC; 23/100), non-invasive ventilation (9/100), invasive mechanical ventilation (24/100), and veno-venous extracorporeal membrane oxygenation (2/100). Prone positioning included awake self-proning in non-ICU patients (4 of 68 patients) and standard proning of ventilated patients in the ICU (13/30). Most ICU patients (24/32) received invasive mechanical ventilation with a median duration of 14 days (IQR 11 to 22).

Twenty-six patients underwent CT thorax scans. The most common findings were bilateral diffuse ground glass opacities, bilateral consolidations, and new fibrosis/bronchiectasis (**Table 3**). Lung ultrasonography (LUS) was performed 30 patients, with the most common abnormalities included thickened, irregular pleural line consistent with an inflammatory process, bilateral alveolar-interstitial syndrome (B-lines), and pulmonary consolidation (**Table 3**). Consolidation on LUS was more likely to be identified in mechanically ventilated patients than in those not on mechanical ventilation (75% vs 33%, $p = 0.025$, OR 6.0, 95% CI 1.17 to 30.73).

Neurologic complications

Table 4 summarizes the short-term neurologic complications among 26 patients (10 non-ICU, 16 ICU) who underwent head CT scanning during hospitalization at the discretion of the treating physician. Three of 26 patients suffered an ischemic stroke, while 6 of 26 patients suffered intracerebral hemorrhage (ICH).

Thrombotic complications & therapies

Thrombotic complications and therapies are shown in **Table 4**. Of the thirteen (4 non-ICU, 9 ICU) who underwent Doppler ultrasound, two ICU patients had a deep venous thrombosis. Twenty-six patients (12 non-ICU and 14 ICU) underwent CT pulmonary angiography at the discretion of the treating physician. Of these, 6 had pulmonary embolism (3 of 68 non-ICU patients and 3 of 32 ICU patients). Eleven (11%) patients received therapeutic anticoagulation during their hospitalization: 3 empirically for suspected COVID-19 associated hypercoagulable state (at the discretion of the treating physician), seven for confirmed venous thromboembolic (VTE) disease, and 1 for ECMO circuit.

Cardiac and hemodynamic complications & therapies

Among 32 ICU patients, 24 (75%) received vasopressor therapy for a median of 7.5 days (IQR 2.3 to 10.8). Four patients received hydrocortisone for refractory shock (**Table 4**). Twenty-nine patients underwent echocardiography during their hospital stay (including both point-of-care and diagnostic). Overall, 4 (13.8%) patients had new left ventricular

dysfunction and 9 (31.0%) patients had new right ventricular (RV) dysfunction (defined as either new systolic failure and/or pulmonary hypertension).

Hepatic complications

Alanine aminotransferase (ALT) levels were used as a surrogate marker for hepatic dysfunction in COVID-19 patients. The highest ALT measured for all study participants during hospital admission was 31 U/L (IQR 22 to 82).

Renal complications & therapies

Twenty-seven (27%) patients (non-ICU: 11/32 [16.1%]; ICU: 16/32 [50%]) developed an acute kidney injury (AKI) defined by Acute Kidney Injury (AKIN) criteria.[10] Among ICU patients, 5 received continuous renal replacement therapy (CRRT) for an average of 4.2 days (SD = 2.59) (**Table 4**). At the time of hospital discharge, 3 of 66 patients (4.5%) had persistent renal injury.

Secondary infections

Fifteen of 100 (15%) patients had an initially negative COVID-19 real-time PCR test, which was subsequently positive on repeat testing. Twelve (12%) patients developed concomitant bacterial respiratory infection, and 1 (1%) patient developed non-Candida fungal respiratory infection. Eight (8%) patients had at least 1 positive blood culture

consistent with non-contaminant bacteremia, and 1 (1%) patient developed *Clostridioides difficile* infection (**Table 4**).

Characteristics of patients who received transfer to ICU after hospital admission

Twelve of 100 patients (12%) were initially admitted to the ward but were subsequently transferred to ICU due to clinical decompensation shortly after hospitalization (median 0.5 days, IQR 0 to 2). Compared to patients who remained in a non-ICU location (n=68), patients transferred to ICU were younger (median 63 years, IQR 53.75 to 68, versus median 76 years, IQR 60.3 to 84.8, $p = 0.01$). Patients initially admitted to a non-ICU location who were later transferred to ICU were more likely to be febrile (≥ 38℃, 75% vs 28.4%, $p = 0.003$) and a have a respiratory rate (RR) ≥ 24 breaths/ minute (72.7% vs. 34.3%, $p = 0.02$) on triage vital signs at presentation to hospital.

Patient Outcomes

Patient outcomes and post-discharge imaging results are shown in **Table 5**. Thirty-four of 100 patients (34%) died in hospital, including 20 of 68 non-ICU patients (29.4%) and 14 of 32 ICU patients (43.8%). Persistent abnormalities were observed in 11 of the 19 patients who had CT scans of the thorax after discharge from hospital (median duration of follow-up 108 days, IQR 41.75 to 187.75). Similarly, 15 patients had repeat echocardiograms after discharge from hospital (duration of follow-up 81 days, IQR 57 to

181), of which one had persistent left ventricular dysfunction and five had persistent right ventricular dysfunction.

Comparing Survivors and Non-Survivors

We compared baseline characteristics of patients who survived to hospital discharge to those who did not. Non-survivors were older (median 80 years [IQR 71.5 to 87.5] vs. 68.5 years [IQR 54.0 to 77.3], $p < 0.01$), more frequently presented with tachycardia (88.9 % vs 24.1%, $p < 0.01$), and more frequently received supplemental oxygen on presentation to ED (50% vs 26.6%, $p = 0.02$). On hospital admission, non-survivors were more frequently acidemic (pH < 7.35) (34.5% vs 17.8%, $p = 0.04$), had a higher white count (10.6 x10^9/L [7.1 to 14.3] vs 6.7 x10^9/L [IQR 4.8 to 8.7], $p < 0.01$), a lower hemoglobin (124 g/L [IQR 113 to 135] vs. 134 g/L [IQR 123.3 to 145.8], $p = 0.03$) and higher troponin (28 ng/L [IQR 14.5 to 75.5] vs. 18 [IQR 8.5 to 29.5], $p < 0.01$).

INTERPRETATION

COVID-19 was initially believed to be an isolated respiratory disease, but emerging reports have suggested that multi-organ involvement may be more common.[3] The full spectrum of organ involvement and their associated outcomes in patients with COVID-19 remain relatively understudied. In this prospective, observational study of hospitalized with COVID-19, we found a range of pulmonary and extra-pulmonary complications in both ICU and non-ICU patients. Patients had a high prevalence of neurologic

complications, thrombotic complications, right ventricular dysfunction, and persistent cardiopulmonary pathology after hospital discharge.

In our study, nearly 10% of patients had a cerebrovascular complication. Other studies reported the prevalence of ischemic stroke to be 2% to 6%,[11, 12] compared to 9% in our cohort. One possible explanation for this phenomenon is that viral infections can result in an inflammatory cascade and endothelial injury that increase the risk of arterial thrombotic events.[13, 14] We also identified intracerebral hemorrhage as a potential sequelae of COVID-19, with 6% of patients of patients developing ICU in our cohort. [15] Intracerebral hemorrhage is hypothesized be due to the binding of SARS-Cov-2 to angiotensin converting enzyme II (ACE-II) receptors on endothelial cells of intracranial blood vessels, resulting in inflammation and disruption of vasculature integrity.[16-18]

In our cohort, thrombotic events (ischemic stroke, deep venous thrombosis, and pulmonary embolism) occurred in 6% of non-ICU patients and 19% in ICU patients. Estimates of thrombotic events in hospitalised patients with COVID-19 have ranged from 5%,[19] to as high as 33%.[20, 21] Several mechanisms, including the complement pathway, neutrophil extracellular traps, inflammatory cytokines, and endothelial dysfunction may explain why patients with COVID-19 could be hypercoagulable.[22, 23] Given the prevalence of thrombotic events, there may be value for routine surveillance as part of the routine clinical care of COVID-19 patients. While there is currently no evidence to support the

routine use of anticoagulation,[24] antiplatelet therapy or systemic therapeutic anticoagulation may hold promise as a treatment for COVID-19, particularly in those with severe disease.[25]

There is a relative paucity of data describing the incidence of right ventricular dysfunction (RVD), manifesting as either and pulmonary hypertension, systolic failure, or dilatation in patients with COVID-19. In one observational study, the prevalence of PH was 12% in hospitalized non-ICU COVID-19 patients.[26] Conversely, we found that 31% of hospitalized patients had evidence of PH. While RV dysfunction has been described in patients with ARDS, the prevalence of RV dysfunction in our study is higher than what has been reported in non-COVID-19 patients with ARDS.[27-29] It is possible that COVID-19 associated RV dysfunction may be pathologically distinct for several reasons. First, macro- and microvascular thrombosis due to deranged coagulation pathways could induce RV dysfunction. Second, 'permissive hypoxia' as a treatment strategy may increase the prevalence of RV dysfunction.[30, 31] Similarly, we found evidence for long-term pulmonary complications associated with COVID-19 beyond hospital discharge. Abnormalities such as bronchiectasis, fibrosis or scarring were found in 57% of patients who underwent CT thorax imaging after hospital discharge for clinical reasons in our cohort. While pulmonary fibrosis has been reported in several small cohorts,[32] our study reinforces the notion that respiratory dysfunction can be prevalent and persistent.

These findings highlight the need to elucidate the true prevalence and potential mechanisms of extra-pulmonary complications associated with COVID-19, particularly neurological, thrombotic, and cardiac manifestations. Future studies should work to identify the patient phenotype where the benefits of anticoagulation will outweigh the risk. The prevalence of acute and long-term RV dysfunction highlights the need to balance the respiratory support from positive pressure ventilation with the adverse mechanical effects it frequently imposes on right ventricular function. Lastly, While the acute inpatient management of COVID-19 has garnered attention among the scientific community, future research should prioritize characterization of the long-term pulmonary and extra-pulmonary complications of COVID-19.

Limitations

Limitations with any observational study such as this one includes the inability to draw any conclusions about the associations of any specific treatment with outcomes. Furthermore, a larger cohort study is required to conduct multivariate analyses. This study has several strengths. We included a cohort of ICU and non-ICU patients across a spectrum of disease severity. Standardized diagnostic microbiologic methods were used to define COVID-19 positivity. Consecutive prospective enrollment reduced selection bias and improved the fidelity of data collection. Furthermore, the prospective nature of our data provides a better understanding of pulmonary and extra-pulmonary

manifestations as well as its management. Finally, we provide post-hospital discharge data on the clinical outcomes of patients after hospital discharge.

Conclusion

In summary, this study provides further evidence that COVID-19 is a multi-system disease that results in neurologic, cardiac, and thrombotic complications in the acute phase as well as pulmonary complications that persist beyond the hospitalization. These findings underscore the need to prioritize research on the long-term outcomes and management of COVID-19 survivors.

Conflicts of Interest: The authors declare no conflicts of interest.

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Contributors: KH and JB conceived and designed the study and oversaw all study conduct. IB, KH, JB, and KB obtained funding for the study. KH, JB, KF, DC, DG, KD, and DL participated in data collection and database management. KH and JB conducted data analysis. KH, JB, KB, MS, and CM prepared the initial draft of the manuscript. All authors contributed to manuscript preparation/ revision, approve the final version to be published and agree to be accountable for all aspects of the work.

Data Sharing Statement: All data will be available upon request.

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Figure 1: Overview of Patient Enrollment and Disposition

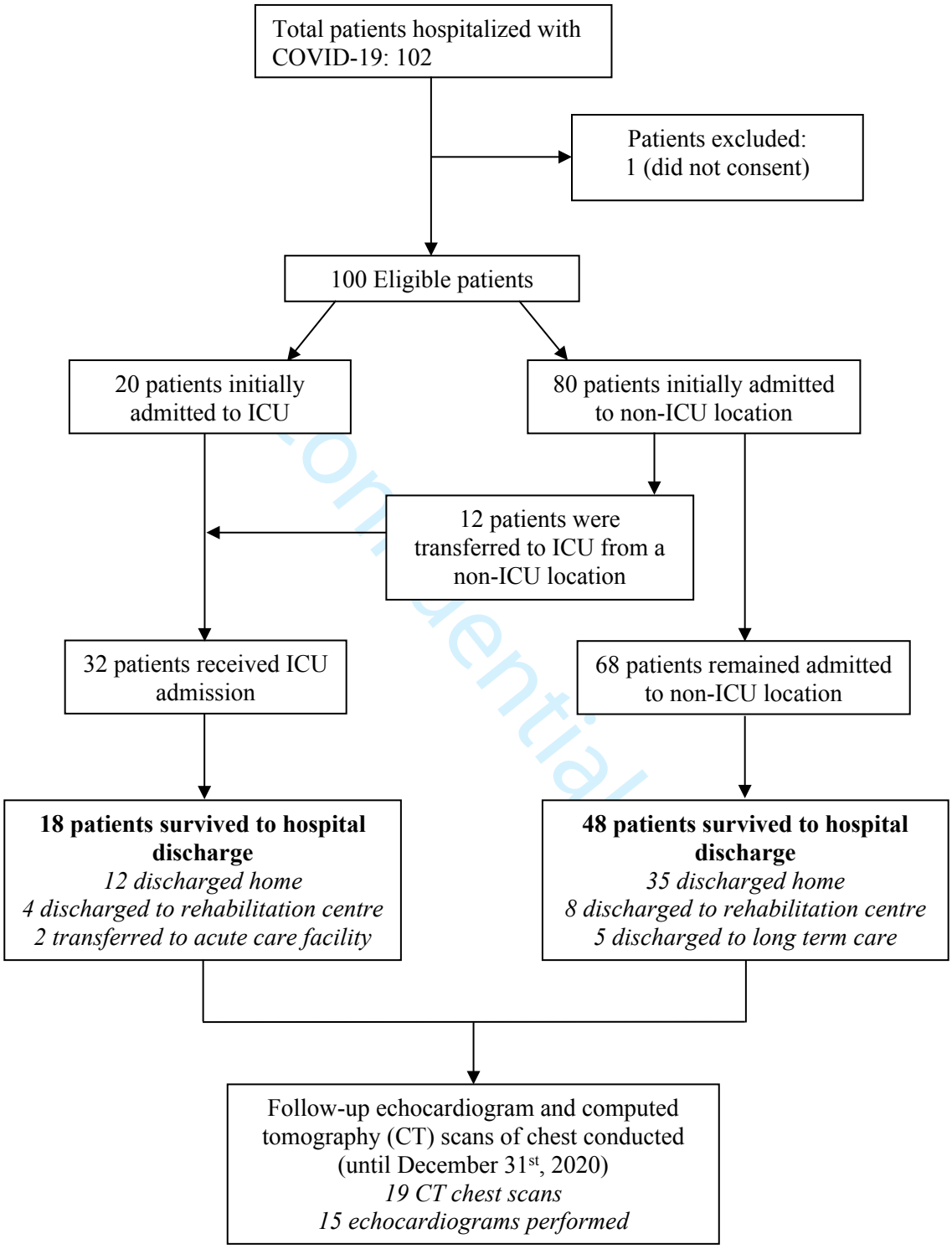

Table 1. Patients' baseline characteristics.

Characteristic	All patients N = 100	Non-ICU patients N = 68	ICU patients N = 32
Demographic Characteristics			
Age - median (IQR)	74 (56,83)	76 (60, 85)	63 (55,74)
Male sex - no (%)	53 (53%)	34 (50.0)	19 (59.4)
Body mass index, mean (SD)	29.2 (8.2) n = 84	28.1 (7.9) n = 56	31.4 (8.5) n = 28
Pre-admission Location - n (%)			
Home	66 (66)	41 (60.3)	25 (78.1)
Long-term care facility	28 (28)	24 (35.3)	4 (12.5)
Retirement home	1 (1)	1 (1.5)	0
Other	5 (5)	2 (2.9)	3 (9.4)
Comorbidities - n (%)			
Chronic cardiac disease	24 (24)	17 (25.0)	7 (21.9)
Chronic pulmonary/ lung disease	17 (17)	14 (20.6)	3 (9.4)
Asthma	15 (15)	10 (14.7)	5 (15.6)
Chronic renal/ kidney disease	15 (15)	10 (14.7)	5 (15.6)
Liver disease	4 (4)	2 (2.9)	2 (6.3)
Chronic neurological disorder	6 (6)	5 (7.4)	1 (3.1)
Cancer [active only]	9 (9)	7 (10.3)	2 (6.3)
History of cancer [in remission]	8 (8)	7 (10.3)	1 (3.1)
Obesity	11 (11)	7 (10.3)	4 (12.5)
Diabetes	30 (30)	19 (27.9)	11 (34.4)
Dementia [any etiology]	16 (16)	15 (22.1)	1 (3.1)
Other comorbidities	7 (7)	5 (7.4)	2 (6.3)
Habits - n (%)			
Current smoker	9 (9)	7 (10.3)	2 (6.3)
Ex-smoker	28 (28)	22 (32.4)	6 (18.8)
Alcohol use	4 (4)	4 (5.9)	0
Illicit drug use	1 (1)	1 (1.5)	0
Exposure History - n (%)			
Contact with confirmed case	30 (30)	23 (33.8)	7 (21.9)
Contact with suspected case	9 (9)	5 (7.4)	4 (12.5)
Travel outside Canada	9 (9)	6 (8.8)	3 (9.4)
Travel within Canada	1 (1)	0	1 (3.1)

ICU: intensive care unit; IQR: interquartile range; SD: standard deviation.

Table 2. Clinical characteristics at the time of presentation to hospital.

Characteristic	All patients N = 100	Non-ICU patients N = 68	ICU patients N = 32
Presenting symptom for > 20% of patients - n (%)			
Cough	71 (71)	50 (73.5)	21 (65.6)
Fever	62 (62)	37 (54.4)	25 (78.1)
Dyspnea	63 (63)	40 (58.8)	23 (71.9)
Fatigue	51 (51)	35 (51.5)	16 (50.0)
Diarrhea	32 (32)	23 (33.8)	9 (28.1)
Myalgia	25 (25)	13 (19.1)	12 (37.5)
Headache	23 (23)	13 (19.1)	10 (31.3)
Vital signs at hospital presentation - n/ N (%)			
Temperature > 38 C	36/ 98 (36.7)	19/ 67 (28.4)	17/31 (54.8)
Heart rate > 100	31/ 96 (32.3)	18/ 66 (27.3)	13/ 30 (43.3)
Systolic blood pressure < 90 mm Hg	3/ 98 (3.1)	2/67 (3.0)	1/ 30 (3.3)
Respiratory rate > 24 breaths/ min	42/ 95 (44.2)	23/ 67 (34.3%)	19/ 28 (67.9)
Oxygen saturation < 92%	20/98 (20.4)	8/ 67 (11.9)	12/ 31 (38.7)
Supplemental oxygen therapy at clinical presentation	35/ 99 (35.4)	18/ 67 (26.9)	17/ 32 (53.1)
Laboratory results at hospital presentation, mean (SD)			
Leukocyte count - $x10^9$/L	10.6 (13.2)	11.0 (15.4)	10.0 (6.1)
Lymphocyte count - $x10^9$/L	3.3 (12.9)	4.2 (15.5)	1.3 (1.3)
Creatinine - umol/L	110.5 (80.1)	106.9 (62.6)	118.5 (110.8)
LDH - U/L	416.3 (253.0)	367.4 (177.5)	563.0 (391.1)
Ferritin - ug/L	1702.6 (2154.4)	1772.1 (2372.3)	1424.4 (998.2)
CRP - mg/L	97.6 (83.5)	87.9 (75.8)	126.8 (101.9)
D-dimer - ug/L	1198.9 (1311.5)	956.0 (789.4)	1603.7 (2093.1)
Troponin - ng/L	31.8 (42.1)	36.3 (46.8)	18.1 (17.5)
Fibrinogen - g/L	7.5 (0.5)	7.4 (0.7)	NA*
pH on blood gas	7.4 (0.1)	7.4 (0.1)	7.4 (0.1)

* one data point only.
ICU: intensive care unit; SD: standard deviation; ER: emergency department; LDH: lactate dehydrogenase; CRP: C-reactive protein.

Table 3. Pulmonary complications and management among hospitalized COVID-19 patients.

Complications & Management	All patients	Non-ICU patients	ICU patients
Clinical parameters			
PF ratio < 150 mm Hg – n (%)	NA	NA	27/ 32 (84.4)
PF ratio < 150 mm Hg – days median (IQR)	NA	NA	8 (4, 15)
CT chest findings - n/ N (%)			
Localized Ground Glass Opacities	4/ 26 (15.4)	3/ 12 (25)	1/ 14 (7.1)
Diffuse Ground Glass Opacities	14/ 26 (53.8)	5/ 12 (41.7)	9/ 14 (64.3)
Unilateral consolidation/infiltration	2/ 26 (7.7)	1/ 12 (8.3)	1/ 14 (7.1)
Bilateral consolidation/infiltration	14/ 26 (53.8)	7/ 12 (58.3)	7/ 14 (50.0)
Unilateral pleural effusion	2/ 26 (7.7)	0/ 12 (0)	2/ 14 (14.3)
Bilateral pleural effusion	3/ 26 (11.5)	2/ 12 (16.7)	1/ 14 (7.1)
Emphysematous changes or bronchiectasis	4/ 26 (15.4)	2/ 12 (16.7)	2/ 14 (14.3)
Scarring or fibrosis	4/ 26 (15.4)	0/ 12 (0)	4/ 14 (28.6)
Organizing pneumonia pattern	2/ 16 (7.7)	1/ 12 (8.3)	1/ 14 (7.1)
Lung Ultrasound Findings - n/ N (%)			
Irregular pleural line	26/ 30 (86.7)	5/ 7 (71.4)	21/ 23 (91.3)
Alveolar-interstitial syndrome (B-lines)	28/ 30 (93.3)	5/ 7 (71.4)	23/ 23 (100)
Consolidation	12/ 30 (40)	0/ 6 (0)	12/ 24 (52.2)
Unilateral	2/ 12 (16.7)	0/ 6 (0)	2/ 12 (16.7)
Bilateral	10/ 12 (83.3)	0/ 6 (0)	10/ 12 (83.3)
Moderate-large pleural effusion	2/ 30 (6.7)	0/ 7 (0)	2/ 23 (8.7)
Respiratory Therapies - n/ N (%)			
Received oxygen therapy	79/ 100 (79)	47/ 68 (69.1)	32/ 32 (100.0)
High-flow nasal cannula	23/ 100 (23)	5/ 68 (7.4)	18/ 32 (56.3)
Non-invasive ventilation	9/ 100 (9)	1/ 68 (1.5)	8/ 32 (25.0)
Mechanical ventilation	24/ 100 (24)	0/ 68 (0)	24/ 32 (75.0)
Duration of mechanical ventilation - days, median (IQR)	NA	NA	14 (10, 22) n=26
Prone positioning	17/ 98 (17.4)	4/ 68 (5.9)	13/ 30 (43.3)
Neuromuscular blocking agents	NA	NA	18/ 32 (56.3)
Steroids for respiratory failure	8/ 100 (8)	4/ 68 (5.9)	4/ 32 (12.5)
VV-ECMO	NA	NA	2/ 32 (6.3)

ICU: intensive care unit; PF ratio: $PaO2/FiO^2$ ratio; IQR: interquartile range; CT: computerized tomography; VV-ECMO: veno-venous extracorporeal membrane oxygenation.

Table 4. Extra-pulmonary complications among hospitalized COVID-19 patients.

Complications & Management	All patients N=100	Non-ICU patients N=68	ICU patients N=32
Neurological complications - n/ N (%)			
Ischemic stroke	3/ 26 (11.5)	1/ 10 (10)	2/ 16 (12.5)
Intracranial hemorrhage	6/ 26 (23.0)	0	6/ 16 (37.5)
Thrombotic complications & therapies - n (%)			
Deep venous thrombosis on ultrasound	2/ 13 (20.0)	0	2/ 9 (22.2)
Pulmonary embolism on CTPA	6/ 25 (24.0)	3/ 11 (27.3)	3/ 14 (21.4)
Received therapeutic anticoagulation	9/ 100 (9)	2/ 68 (2.9)	7/ 32 (21.9)
Started for presumed hypercoagulable state due to COVID-19	3/ 100 (3)	0	3/ 32 (9.4)
Started for confirmed venous thromboembolism	5/ 100 (5)	2/ 68 (2.9)	3/ 32 (9.4)
Started for VV-ECMO circuit	1/ 100 (1)	0	1/ 32 (3.1)
Cardiac & hemodynamic complications & therapies			
Received vasopressors or inotropes - n (%)	NA	NA	24 (75.0)
Duration of vasopressors or inotropes - days, median (IQR)	NA	NA	7.5 (2.3, 10.8) n=26
Steroids for hemodynamic shock - n (%)	4 (4.0)	0	4 (12.5)
Echocardiogram findings - n/ N (%)			
Depressed LVEF (30-50%)	2/ 29 (6.9)	0/ 5 (0)	2/ 24 (8.3)
Severely depressed LVEF (< 30%)	2/ 29 (6.9)	1/ 5 (40)	1/ 24 (4.2)
Reduced RV systolic function	5/ 29 (14.8)	1/ 5 (20)	3/ 24 (12.5)
Pulmonary hypertension	9/ 29 (31.0)	2/ 5 (40)	7/ 24 (29.2)
Pericardial effusion	1/ 29 (3.4)	0/ 5 (0)	1/ 24 (4.2)
Renal complications & therapies			
Acute kidney injury - n (%)	27 (27)	11 (16.1)	16 (50)
Received CRRT - n (%)	NA	NA	5 (15.6)
Duration of CRRT - mean (SD)	NA	NA	4.2 (2.59)
Highest AKIN stage - n (%)			
Stage I	16 (16)	9 (13.2)	7 (21.9)
Stage II	5 (5)	0	5 (15.6)
Stage III	6 (6)	2 (2.9)	4 (12.5)
Secondary infections - n (%)			
Positive respiratory culture	13 (13.0)	0	13 (40.6)
Positive blood culture	8 (8.0)	2 (2.9)	6 (18.75)
Positive urine culture	15 (15.0)	4 (5.9)	11 (34.4)
Clostridium difficile	1 (1.0)	1 (1.5)	0

ICU: intensive care unit; IQR: interquartile range; SD: standard deviation; CTPA: computerized tomography pulmonary angiography; VV-ECMO: veno-venous extracorporeal membrane oxygenation; LVEF: left ventricular ejection fraction; RV: right ventricle; CRRT: continuous renal replacement therapy; AKIN: Acute Kidney Injury Network.

Table 5. Outcomes of hospitalized patients with COVID-19.

Outcome	All patients N = 100	Non-ICU patients N = 68	ICU patients N = 32
Vital status - n (%)			
28-day mortality	28 (28.0)	15 (22.1)	13 (40.6)
Hospital mortality	34 (34.0)	20 (29.4)	14 (43.8)
Disposition among survivors - n/ N (%)			
Another acute care facility	2/ 66 (3.0)	0	2/ 18 (11.1)
Rehabilitation centre	12/ 66 (18.2)	8/ 48 (16.7)	4/ 18 (22.2)
Home	47/ 66 (71.1)	35/ 48 (72.9)	12/ 18 (66.7)
Long-term care facility	5/ 66 (7.6)	5/ 48 (10.4)	0
CT thorax findings after hospital discharge - n/ N (%)			
Ground glass opacities	5/ 19 (26.3)	3/ 11 (27.3)	2/ 8 (25.0)
Emphysematous or bronchiectatic	6/ 19 (31.6)	2/ 11 (18.2)	4/ 8 (50.0)
Scarring or fibrosis	5/ 19 (26.3)	0/ 11 (0)	5/ 8 (62.5)
Echocardiogram finding after hospital discharge - n/ N (%)			
Depressed LVEF (30-50%)	1/ 15 (6.7)	1/ 10 (10.0)	0/ 5 (0)
Reduced RV systolic function	2/ 15 (13.3)	2/ 10 (20.0)	0/ 5 (0)
Right ventricular dilatation	5/ 15 (33.3)	3/ 10 (30.0)	2/ 5 (40.0)

ICU: intensive care unit; CT: computerized tomography; LVEF: left ventricular ejection fraction; RV: right ventricle.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 2 2, 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5, Supplementary Online Material 1
Bias	9	Describe any efforts to address potential sources of bias	NR
Study size	10	Explain how the study size was arrived at	NR
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	7, Tables 1 & 2
Outcome data	15*	Report numbers of outcome events or summary measures over time	11, 12, Table 5

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-11, Tables 3 & 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15, 16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.