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Research

Characteristics and outcomes of patients with COVID-19 admitted to hospital and intensive care in the first phase of the pandemic in Canada: a national cohort study

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Abstract

Background: Clinical data on patients admitted to hospital with coronavirus disease 2019 (COVID-19) provide clinicians and public health officials with information to guide practice and policy. The aims of this study were to describe patients with COVID-19 admitted to hospital and intensive care, and to investigate predictors of outcome to characterize severe acute respiratory infection.

Methods: This observational cohort study used Canadian data from 32 selected hospitals included in a global multisite cohort between Jan. 24 and July 7, 2020. Adult and pediatric patients with a confirmed diagnosis of COVID-19 who received care in an intensive care unit (ICU) and a sampling of up to the first 60 patients receiving care on hospital wards were included. We performed descriptive analyses of characteristics, interventions and outcomes. The primary analyses examined in-hospital mortality, with secondary analyses of the length of hospital and ICU stay.

Results: Between January and July 2020, among 811 patients admitted to hospital with a diagnosis of COVID-19, the median age was 64 (interquartile range [IQR] 53–75) years, 495 (61.0%) were men, 46 (5.7%) were health care workers, 9 (1.1%) were pregnant, 26 (3.2%) were younger than 18 years and 9 (1.1%) were younger than 5 years. The median time from symptom onset to hospital admission was 7 (IQR 3–10) days. The most common symptoms on admission were fever, shortness of breath, cough and malaise. Diabetes, hypertension and cardiac, kidney and respiratory disease were the most common comorbidities. Among all patients, 328 received care in an ICU, admitted a median of 0 (IQR 0–1) days after hospital admission. Critically ill patients received treatment with invasive mechanical ventilation (88.8%), renal replacement therapy (14.9%) and extracorporeal membrane oxygenation (4.0%); 26.2% died. Among those receiving mechanical ventilation, 31.2% died. Age was an influential predictor of mortality (odds ratio per additional year of life 1.06, 95% confidence interval 1.03–1.09).

Interpretation: Patients admitted to hospital with COVID-19 commonly had fever, respiratory symptoms and comorbid conditions. Increasing age was associated with the development of critical illness and death; however, most critically ill patients in Canada, including those requiring mechanical ventilation, survived and were discharged from hospital.

A chief concern over the first months of the coronavirus disease 2019 (COVID-19) pandemic was the capacity to provide care for acutely ill patients in hospitals and intensive care units (ICUs). The variability in outcomes of patients with COVID-19 internationally has been striking, with some reports describing ICU mortality in ranges between 40 and 90%.[1–3] Systematic reviews including

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10 000 patients worldwide show a combined ICU mortality of 42%.[4] Acute care features associated with mortality include health care resource use and availability, supportive care and specific treatment strategies.[5,6]

Canada has had more than 10 000 hospital admissions for COVID-19 and 110 000 confirmed cases as of July 15, 2020, the time of this data analysis.[7] These hospital admissions have resulted in health system strain — particularly in acute care and long-term care homes; however, hospitals and ICUs have not been overwhelmed to the extent experienced in many other countries,[1,8] perhaps owing to public health strategies that have included physical distancing and border closures, effective hospital-based infection prevention and control practices, early cessation of nonemergent care and luck.

Documenting the numbers and characteristics of patients with COVID-19 requiring hospital or ICU admission across Canadian hospitals is vital to facilitate comparison with other health jurisdictions and in preparation for future pandemic waves. We aimed to describe a representative population of patients with COVID-19 admitted to hospital and intensive care, and investigate predictors of outcome using a national pre-existing registry to characterize severe acute respiratory infection.

Methods

Study design

SPRINT-SARI (Short Period Incidence Study of Severe Acute Respiratory Infection) is a global, multisite observational cohort of patients admitted to hospital with severe acute respiratory infection.[9] Data have been collected in Canada and across the world since 2016, establishing research infrastructure for pandemics to rapidly produce observational data.[10]

In January 2020, the case report form was adapted for COVID-19, and has been used, in conjunction with the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and the World Health Organization (WHO), around the world to describe clinical disease from COVID-19 across populations and inform policy globally.[11–13] SPRINT-SARI is administered in Canada from Sunnybrook Research Institute with a global data repository coordinated by the University of Oxford, which included more than 100 000 patients as of July 2020.

Data sources

Participating Canadian sites were recruited through convenience sampling, both through the Canadian Critical Care Trials Group, a national trials network, and through networks of the research team, and included both pediatric and adult hospitals across the country with both academic and community hospitals (Appendix 1, available at www.cmajopen.ca/content/9/1/E181/suppl/DC1). There was no specific geographic targeting or specific sampling strategy employed. These data from Canadian hospitals are included in global data sets, including the relevant research tools such as case report forms;[14] these data will also be included in global analyses that will be forthcoming.

Participants

The study population included all patients with a confirmed diagnosis of COVID-19 who were admitted to an ICU in study hospitals, as well as quota sampling of up to the first 60 patients admitted to hospital wards between Jan. 24 and July 7, 2020. This sampling strategy was meant to more comprehensively sample critically ill patients and to limit data collection by strained research and clinical teams during the first wave of the pandemic.

Data were collected on admission, daily and on hospital discharge, and included baseline demographic characteristics, comorbidities, interventions given and hospital outcomes. Data elements were standardized with global data collection efforts with ISARIC and the WHO to optimize international comparisons. ICUs were defined as per local practice, acknowledging that the capabilities and capacities of ICUs vary across hospitals. Comorbidities were defined by the treating clinicians as documented in patient charts. Patients were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) according to local practice, which was naso- or oropharyngeal swabs for polymerase chain reaction testing at all centres, and patients received treatment according to local standards of care.

Statistical analysis

The primary outcome measure was in-hospital mortality censored as of July 7, 2020. Secondary outcomes included duration of ICU and hospital stay. Unadjusted odds ratios (ORs) for mortality with baseline demographic characteristics, including age and comorbidities, were calculated by univariate analysis. Descriptive statistics included frequency analysis (percentages) for categorical variables, and means (standard deviation [SD]) or medians (interquartile range [IQR]) for continuous variables, depending on data distribution.

We performed logistic regression modelling for the primary outcome, using baseline age and sex as the adjusted variables based on data from other cohorts. Data were submitted and checked for errors by manual inspection and electronic range limits. We evaluated symptoms for pairwise comparisons. Patients still alive and in hospital at the time of censoring were not included in the outcome assessments. We used the Kaplan–Meier method to depict the probability of survival over the duration of follow-up and to generate survival curves, with bounds as 95% confidence intervals (CIs). Estimates for distribution of time-based variables were obtained through a γ distribution fitted onto the observed data, accounting for unobserved outcomes, with estimation by a maximum likelihood procedure and CIs for the means and variances obtained by bootstrap. Confidence intervals and p values reported reflect a 2-tailed α level of 0.05. Statistical analyses were performed in R.[15]

Ethics approval

This study was approved by local ethics boards, generally using a waiver of consent given the need to collect routinely

available clinical data only, with no need for additional study-specific diagnostic testing.

Results

From Jan. 24 until July 7, 2020, 811 hospital-admitted patients across 32 hospitals (4 academic pediatric, 13 community and 15 adult academic) were included in the analysis. Of these, 328 patients required admission to an ICU.

The median age of all patients was 64 (IQR 53–75) years, 495 (61.0%) were men, 9 (1.1%) were pregnant and 46 (5.7%) were health care workers. A total of 26 (3.2%) were younger than 18 years and 9 were younger than 5 years (Table 1), with 5 children being admitted to ICUs in participating children's hospitals.

Presenting symptoms are described in Figure 1; the most common symptoms on admission were fever (593/804, 73.7%), shortness of breath (538/802, 67.1%), cough (331/680, 48.6%), fatigue or malaise (347/801, 43.3%), and diarrhea (209/800, 26.1%). Mapping symptoms into clusters revealed no clear patterns of symptoms, and less than 7% of patients presented without one of fever, shortness of breath, fatigue or cough. The median time from symptom onset to hospital admission was 7 (IQR 3–10) days.

Table 1, Figure 2, and Appendix 2, Supplemental Figure 2 (available at www.cmajopen.ca/content/9/1/E181/suppl/DC1) show the most common comorbidities, including diabetes, hypertension, and cardiac, kidney and respiratory disease. With regard to outpatient medications, 90 (11.1%) patients were taking nonsteroidal anti-inflammatory drugs, 104 (12.8%) were taking angiotensin-converting enzyme inhibitors and 122 (15.0%) were taking angiotensin receptor blockers.

Treatments

Most patients received antibiotics (78.9%) or oxygen (74.2%). In total, 21.2% of patients received an antiviral agent, with oseltamivir, lopinavir–ritonavir, hydroxychloroquine and ribavirin being the 4 most commonly used; 18.6% of ward patients and 28.9% of ICU patients received systemic corticosteroids (Table 2).

Patients were admitted to ICU a median of 0 (IQR 0–1) days after admission to hospital, with 58.8% on the first day of hospital admission and 75.9% of patients within the first 2 days

Table 1: Characteristics of patients with coronavirus disease 2019 admitted to hospital and intensive care

Characteristic	No. (%)*	
	All patients admitted to hospital *n* = 811	Patients admitted to ICU *n* = 328†
Age, yr, median (IQR)	64 (53–75)	65 (54–72)
Age, yr		
< 19	26 (3.2)	5 (1.5)
> 70	40 (4.9)	23 (7.0)
Sex, female‡	315 (38.8)	105 (32.0)
Comorbidities		
Hypertension	361 (44.5)	149 (45.4)
Diabetes	203 (25.0)	90 (27.4)
Cardiac disease	171 (21.1)	67 (20.4)
Chronic kidney disease	102 (12.6)	67 (20.4)
Liver disease	30 (3.7)	14 (4.3)
Asthma	90 (11.1)	38 (11.6)
Smoking	37 (4.6)	16 (4.9)
Obesity	23 (2.8)	15 (4.6)
AIDS/HIV	8 (1.0)	3 (0.9)
Malignant neoplasm	28 (3.5)	13 (4.0)
Pregnancy	12 (1.5)	0
Time from symptom onset to hospital admission, d, mean ± SD	12.5 ± 8.8	15.0 ± 9.3
Overall mortality	166 (20.5)	86 (26.2)

Note: ICU = intensive care unit, IQR = interquartile range, SD = standard deviation.
*Unless stated otherwise.
†Of the 811 patients in hospital, 328 were admitted to ICU and 483 were treated on the ward.
‡Sex was unreported in 1 patient.

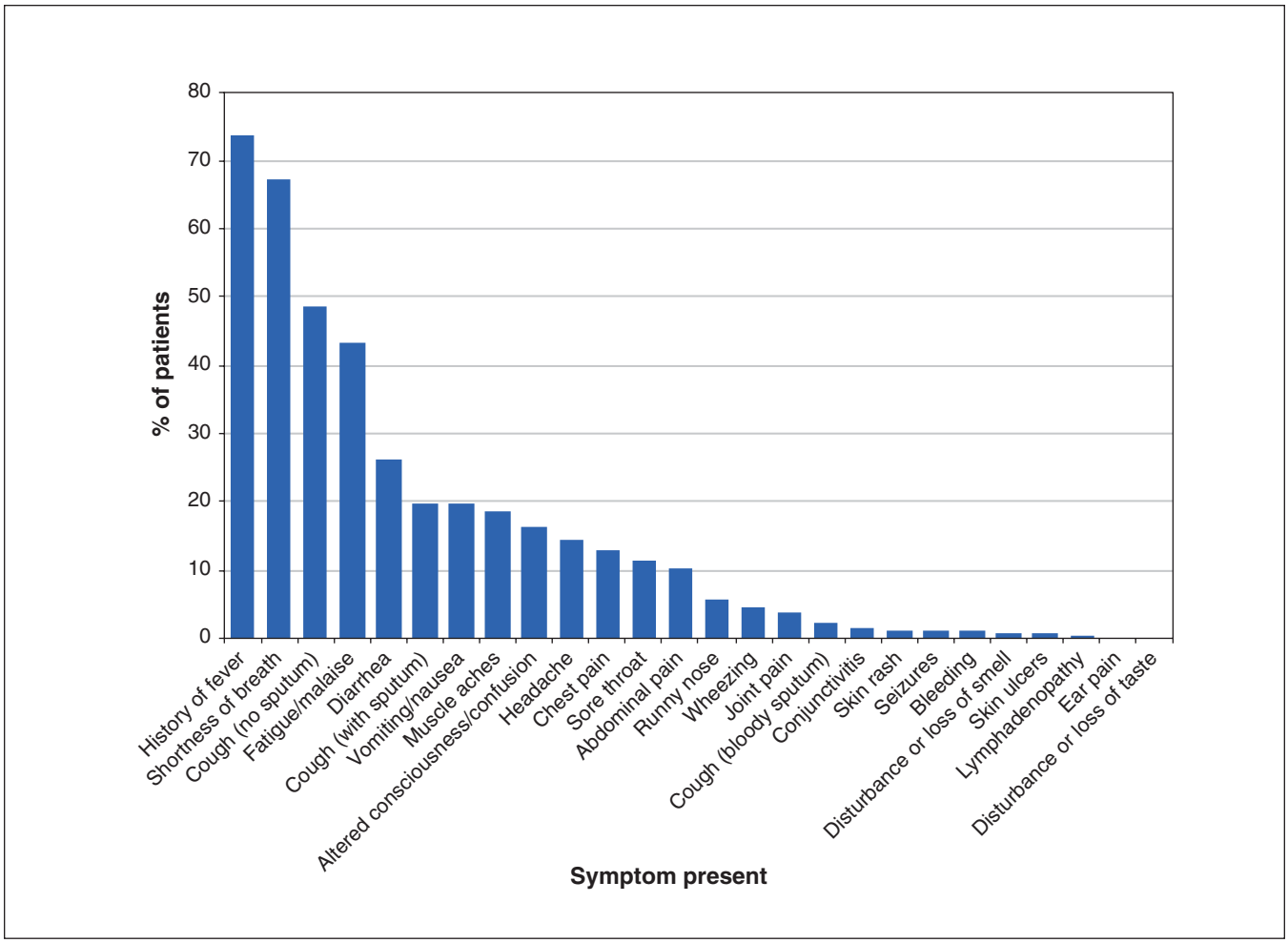

Figure 1: Presenting symptoms seen on admission among 811 patients admitted to hospital with coronavirus disease 2019.

of hospital admission. Appendix 2, Supplemental Figure 1 shows length of stay by sex, age and admission location. Appendix 2, Supplemental Figure 3 shows the density function of time to outcome (death or recovery) in included patients.

Outcomes

As of reporting, 166 patients had died (20.5%) (Figure 3). Of the 328 patients admitted to an ICU, 86 (26.2%) had died, with 20 patients (2.5%) still admitted to hospital as of July 7, 2020. Seven deaths occurred in patients younger than 50, with the youngest death at age 27 (Table 3). Each additional year of age was independently associated with death on univariate analysis (OR 1.06, 95% CI 1.03–1.09). A total of 80 hospital-admitted patients died without having been admitted to an ICU (48.2% of all deaths), suggesting limitations on care were present.

Mortality among patients who received invasive mechanical ventilation was 31.2%, 69.2% among patients receiving ECMO and 46.9% among those who received renal replacement therapy during their ICU course. Patients who died were also more likely to have comorbidities (Table 3), including hypertension (OR 2.52, 95% CI 1.70–3.78), chronic pulmonary disease (OR 3.11, 95% CI 1.93–4.99), chronic renal disease (OR 2.31, 95% CI 1.43–3.69), diabetes (OR 2.28, 95% CI 1.50–3.45), or a malignant neoplasm (OR 2.31, 95% CI 1.18–4.42). Multivariate modelling, adjusting for age and sex, showed that chronic pulmonary disease (OR 3.45, 95% CI 1.13–10.73) and chronic renal disease (OR 3.88, 95% CI 1.15–13.8) were the comorbidities strongly predictive of in-hospital mortality.

Interpretation

We report on a large cohort of Canadian patients admitted to hospital with COVID-19 (representing about 8% of all admitted patients in Canada at the time [total 10 728] and 14.6% of all ICU admissions [total 2247][7]). We describe demographic data, interventions and clinical outcomes of patients. The most common presenting symptoms were fever and cough, and the most common comorbidities were hypertension, diabetes and chronic cardiac disease. Among patients admitted to hospital with COVID-19 who received intensive care, mortality was 26%, similar to reports from other regions of the world.[1,16–19]

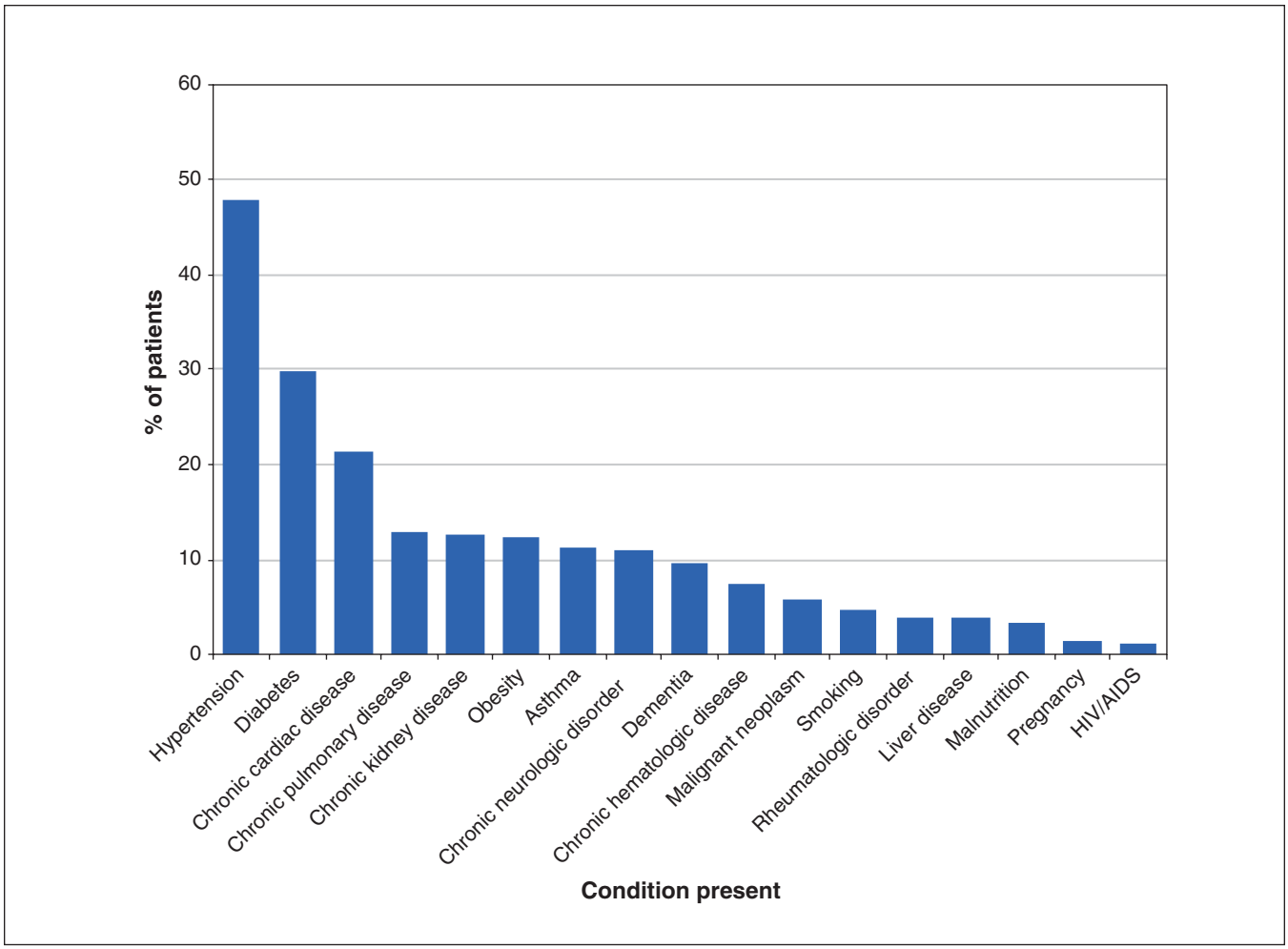

Figure 2: Presenting comorbidities at admission among 811 patients admitted to hospital with coronavirus disease 2019.

Table 2: Interventions received among ward or critically ill patients with coronavirus disease 2019

Treatment	No. (%)	
	Ward patients *n* = 483	ICU patients *n* = 328
Antibiotics	357 (73.9)	283 (86.3)
Antiviral agent	96 (19.9)	76 (23.2)
Systemic corticosteroids	90 (18.6)	95 (29.0)
Oxygen	274 (56.7)	328 (100)
High-flow nasal oxygen	65 (13.5)	40 (12.2)
Noninvasive ventilation	19 (3.9)	35 (10.7)
Invasive ventilation	–	291 (88.7)
Prone ventilation	–	55 (16.8)
Inotropes or vasopressors	–	274 (83.5)
Renal replacement therapy	–	49 (14.9)
ECMO	–	13 (4.0)
Tracheostomy	–	10 (3.0)

Note: ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit.

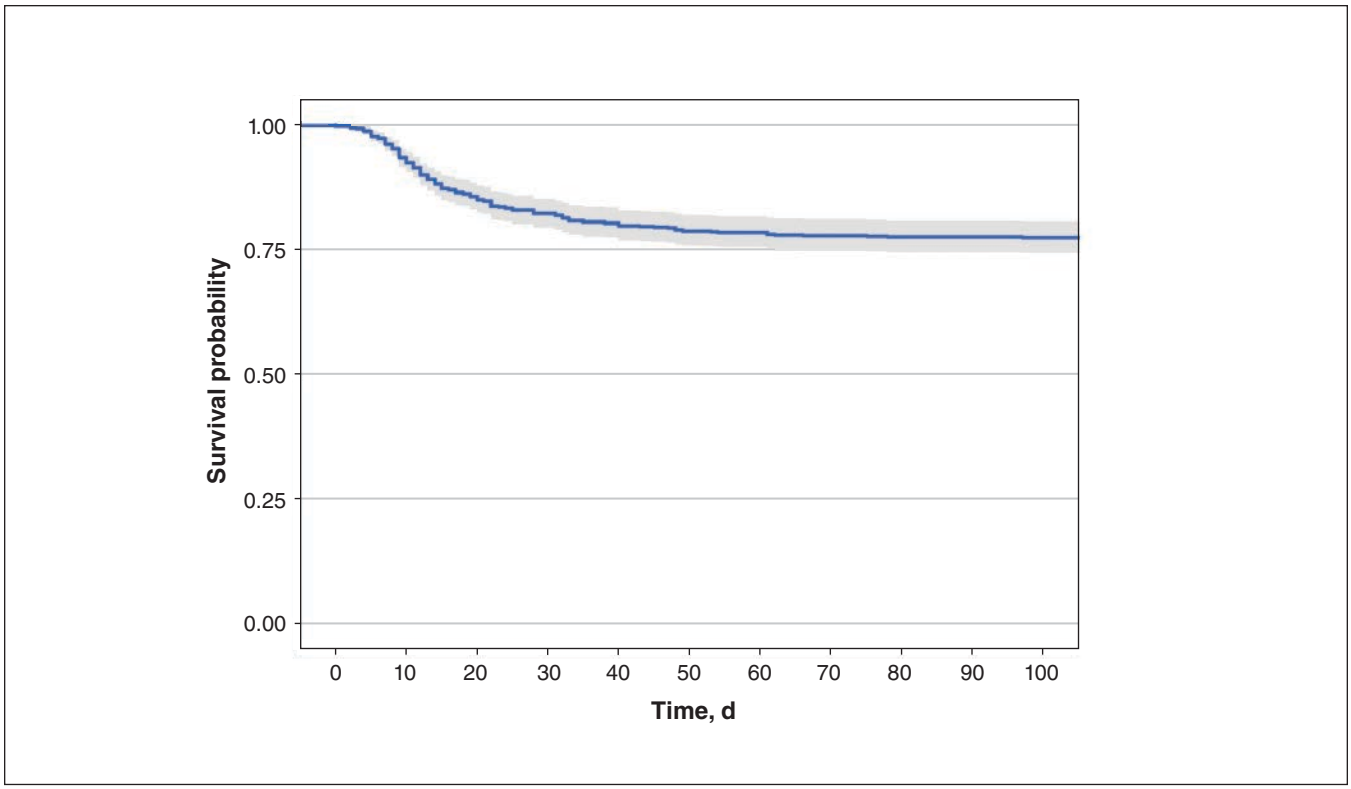

Figure 3: Time-to-event analysis for mortality. Shaded bars represent 95% confidence intervals.

Among patients admitted to the ICU, or those requiring mechanical ventilation, mortality was lower in our study than reported in many other countries in earlier phases of the pandemic.[1,4] The reasons for this difference are not clear and might reflect differing demographic characteristics across studies, the impact of limited capacity for some elements of critical care during periods of greatest COVID-19-related health system stress, differences in admission decisions or treatments, publication bias or other factors. The association of worse outcomes with older age has been previously shown; and differences in the ages of published cohorts may explain a high degree of variation in country-based case-fatality rates.[20] Comparing with previous years in the same data collection exercise, there was about a 10% mortality rate for ICU patients with severe acute respiratory infection.[9] We were unable to capture the presence of do-not-resuscitate or withdrawal of life-sustaining therapy orders and patient preferences, which may differ across the lifespan, and their impact on outcomes.

Less than 7% of patients presented without fever, shortness of breath, or fatigue or cough, similar to other cohorts.[17] Standard screening practices focused on respiratory symptoms in hospitals in Canada are likely to remain relevant.

There were few children and pregnant women in this cohort. The small number of children is in keeping with findings elsewhere, where severe pediatric disease is relatively rare. Given the small numbers of children and pregnant women, we cannot make inferences about typical clinical characteristics or outcomes in these populations.[21] Large-scale international collaboration is required for a better understanding of the health effects on these groups.

There has been uncertainty regarding optimal methods of oxygenation and ventilation support for critically ill patients with COVID-19, which likely has influenced their infrequent use in this cohort. Uncertainty has surrounded the timing of intubation and mechanical ventilation, and the potential risk to health care workers in using noninvasive ventilation and high-flow nasal oxygen, stemming from concern of aerosolization and nosocomial amplification of SARS-CoV-2 transmission.[22] We have not examined the association of specific medication or ventilation treatments with clinical outcomes owing to the inability to adequately adjust for confounding, immortal time and treatment indication bias in observational studies such as this one.

Limitations

The limitations of this study include the scope and granularity of data collected, and the sampling strategies. The study was meant to be rapidly deployed, scalable and operational at sites with varying research infrastructure, and we have collected a minimal clinical data set across Canadian hospitals. This has allowed SPRINT-SARI to continue without prepandemic funding, minimizing the data collection burden at individual sites. We have not reported laboratory data in this report owing to a large degree of missing data, limiting analysis. Some uncertainty will exist on long-term outcomes, which are better characterized through population-level studies, as some patients have not had their final outcome

Table 3: Characteristics of patients with coronavirus disease 2019 who died or survived*

Characteristic	No. (%)†		p value
	Patients who survived n = 625	Patients who died n = 166	
Age, yr, mean ± SD	50.4 ± 25.6	71.7 ± 11.9	< 0.001
Age, yr			
< 18	26 (100)	0	
19–39	75 (96.1)	3 (3.8)	
40–59	180 (88.2)	24 (11.7)	
60–79	316 (82.5)	67 (17.5)	
≥ 80	48 (40.0)	72 (60.0)	
Sex			
Female	234 (37.5)	73 (43.9)	0.2
Male	391 (62.5)	93 (56.1)	
Comorbidities			
Hypertension	264 (73.1)	97 (26.9)	
Diabetes	148 (72.9)	55 (27.1)	
Chronic kidney disease	68 (66.6)	34 (33.3)	
Asthma	67 (74.4)	23 (25.6)	
Smoking	25 (67.5)	12 (32.4)	
Pregnancy	12 (100)	0	
Time from symptom onset to hospital admission, d, mean ± SD	6.9 ± 12.4	3.9 ± 16.3	0.04
Length of stay in hospital, d, mean ± SD	15.9 ± 20.1	16.4 ± 22.2	0.8

Note: SD = standard deviation.
*As of reporting (July 7, 2020), 20 patients were still admitted to hospital.
†Unless stated otherwise.

declared or may have died after discharge to a long-term care facility.

Symptom characterization was dependent on patient report or clinician charting — for example, the low rate of anosmia is likely in keeping with its lack of recognition early in the pandemic or in patients who were too sick to report it. More in-depth characterization of disease, of specific subgroups of patients, and of resource use will require more thorough data collection at each site, including risk-adjustment with standardized data.[23] Sampling was via convenience sampling for hospitals, and quota sampling within hospitals, and may not be representative of the Canadian population, more broadly.

The lack of interprovincial prepandemic capacity for this work underscores the need for a national clinical characterization data infrastructure for hospital-admitted patients that is rapidly accessible for Canadian clinicians, researchers, public health officials and policy-makers to inform understanding of the baseline characteristics, risk factors for outcomes and hospital use, and for benchmarking of disease severity over waves of outbreaks and across different care systems. This system would have value in both the inter- and intrapandemic periods.

Conclusion

We report clinical characteristics and outcomes of 811 patients admitted to hospital during the first wave of the COVID-19 pandemic in Canada. These data are crucial to expand during future pandemic waves to understand the impact of COVID-19 on our hospitals, to identify areas for improvements in clinical management, and to allow for ongoing international and temporal comparisons of outcomes for patients with COVID-19.

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