

Research

Outcomes of hospital-acquired SARS-CoV-2 infection in the Canadian first wave epicentre: a retrospective cohort study

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Abstract

Background: During the first wave of the COVID-19 pandemic, a substantial number of Quebec hospitals were hit by hospital-acquired (HA) SARS-CoV-2 infections. Our objective was to assess whether mortality is higher in HA cases than in non-hospital-acquired (NHA) cases and determine the prevalence of HA-SARS-CoV-2 infection in our hospital.

Methods: This retrospective single-centre cohort study included all adults (≥ 18 yr) who had COVID-19, admitted to Hôpital Maisonneuve-Rosemont (Montréal, Canada) from Mar. 1 to June 30, 2020. We collected data on demographic characteristics, comorbidities, treatment, admission to the intensive care unit (ICU) and mechanical ventilation requirements from electronic health records. We adjudicated hospital acquisition based on the timing of symptom onset, and polymerase chain reaction testing for and exposures to SARS-CoV-2. To evaluate the association between HA-SARS-CoV-2 infection and in-hospital mortality, we computed a multivariable logistic regression analysis including known risk factors for death in patients with COVID-19 as covariates.

Results: Among 697 patients with SARS-CoV-2 infection, 253 (36.3%) were classified as HA. The mortality rate was higher in the HA group than in the NHA group (39.1% v. 25.9%, p = 0.001), while the rates of ICU admission (8.3% v. 19.1%, p = 0.001) and requirement for mechanical ventilation (3.6% v. 13.0%, p = 0.001) were lower. Multivariable logistic regression analysis showed that HA-SARS-CoV-2 infection in patients younger than 75 years is an independent risk factor for death (odds ratio 2.78, 95% confidence interval 1.44-5.38).

Interpretation: Our results show that HA-SARS-CoV-2 infection in younger patients was associated with higher mortality. Future studies need to evaluate relevant patient-centred long-term outcomes in this population.

s of January 2022 in Canada, about 2300000 cases of COVID-19 have been confirmed since the beginning of the pandemic, with more than 30500 deaths.1 During the first wave of this pandemic (first half of 2020), the province of Quebec, whose population was nearly 8.5 million as of January 2021,² had the highest number of COVID-19 cases compared with other provinces. Montréal was the epicentre, accounting for more than one-third of all cases in the province.3 In the first wave of the pandemic, about 10% of patients who developed COVID-19 in Wuhan, China, required admission to hospital and 5% required admission to the intensive care unit (ICU).^{4,5} Older patients and those with existing comorbidities are at higher risk of adverse outcomes.⁵

Amid this pandemic, hospitals have tried to continue their usual activities and provide urgent care. Unfortunately, hospital admission represents a potential environment for viral transmission to vulnerable patients.6 As of February 2021, there were mixed data about outcomes for patients with hospital-acquired (HA) SARS-CoV-2 infection compared with non-hospital-acquired (NHA) infection, as well as inhospital transmission dynamics of SARS-CoV-2. Some studies showed a case fatality rate as high as 36% for patients with HA-COVID-19,7 while others reported a mortality rate lower than that of patients with NHA-COVID-19.8

Therefore, we aimed to assess whether mortality and complications were increased in HA cases of SARS-CoV-2 infection when compared with NHA cases at Hôpital Maisonneuve-Rosemont. We also explored the role of patients sharing multi-bed rooms in hospital with respect to in-hospital transmission of SARS-CoV-2.

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Methods

Study design and setting

We conducted a retrospective cohort study through chart review at Hôpital Maisonneuve-Rosemont — a tertiary academic hospital built in 1954 and hosting 544 beds, including 16 ICU beds — in Montréal, Canada. On Mar. 20, 2020, it was designated as a COVID-19 care centre by the Quebec Ministry of Health and Social Services, and thereafter received transfers from other institutions. Before this date, most patients with COVID-19 who presented to our centre had been transferred to other hospitals. During the first wave of the pandemic (Jan. 25 to June 30, 2020), up to 191 designated beds for patients with confirmed COVID-19 were made available in our centre, including 19 ICU beds. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.⁹

Participants

Our analysis included all patients with confirmed SARS-CoV-2 infection aged 18 years or older who had been admitted to our hospital from Mar. 1 to June 30, 2020. We excluded patients with a diagnosis of COVID-19 more than 2 weeks before hospital admission. The list of all patients with SARS-CoV-2 infection was provided by the hospital Infection Prevention and Control (IPAC) division, which prospectively tracked all inpatients and outpatients positive for the virus via polymerase chain reaction (PCR) testing in our institutions, based on the local laboratory data and data from other institutions for patient transfers. The IPAC division includes certified infection control practitioners, supervised by a medical director. We then cross-matched this list with our hospital administrative data set to determine which patients had been admitted to hospital.

Data sources

We created and managed a data abstraction form using Research Electronic Data Capture (REDCap).¹⁰ Two senior residents (A.B. and E.M.) and 2 research nurses performed data collection. The 2 residents supervised the research nurses throughout the project and performed accuracy checks throughout data collection. Although we did not perform formal reliability testing, most errors occurred only during the first weeks of the collection process.

We gathered data on demographic characteristics, place of origin before hospital admission, deprivation index based on postal code, 11 and comorbidities based on the Charlson Comorbidity Index score, 12 as well as the need for mechanical ventilation and ICU admission. We also collected information on specific drug therapies, such as hydroxychloroquine, azithromycin, tocilizumab, corticosteroids (defined as any dose higher than adrenal insufficiency supplementation dose) and lopinavir-ritonavir. We did not compile information on anticoagulation prescriptions, as this drug class was not considered as a potential therapy at the time of data collection.

Case definitions

SARS-CoV-2 infection was defined as at least 1 positive SARS-CoV-2 PCR test (combined throat and nasopharyngeal swab or lower respiratory tract aspiration). We used the date of the first positive test if multiple tests were performed. We then classified cases as HA or NHA using definitions from the Institut National de Santé Publique du Québec (INSPQ).¹³ Proven HA cases were defined as a positive SARS-CoV-2 PCR test more than 14 days after hospital admission or when an in-hospital epidemiologic link was identified with a person known by the IPAC division to have SARS-CoV-2 infection. The medical director of IPAC made all final attributions based on epidemiologic links, using best clinical judgment without being aware of each patient's outcome. We defined suspected HA cases as occurring 7 to 14 days after hospital admission. We defined NHA cases as those occurring fewer than 7 days after hospital admission, including infections acquired in the community and longterm care facilities or any other congregate living settings. For our analysis, we combined proven and suspected HA cases as HA cases, to match other published studies.^{7,14}

Infection prevention and control and testing practices

Infection prevention and control practices, visitor restrictions and testing practices changed during the pandemic's first wave, reflecting evolving knowledge and scaling-up of SARS-CoV-2 PCR testing availability (Appendix 1, eTable 1, available at www.cmajopen.ca/content/10/1/E74/suppl/DC1). Patients with COVID-19 and those admitted for another reason who were also found to be positive for SARS-CoV-2 infection were admitted to designated COVID-19 wards.

Droplet and contact precautions were required when caring for patients with suspected or confirmed SARS-CoV-2 infection, with personal protective equipment (PPE) including procedure mask, eye protection, isolation gown and gloves. N95 respirators were reserved for aerosol-generating medical procedures or patients presenting with predefined severity criteria concordant with INSPQ guidelines. However, our hospital was affected by PPE and hand sanitizer shortages, leading to a suboptimal uptake of some IPAC practices. Symptomatic health care workers and those with high levels of exposure to a person known to be positive for SARS-CoV-2 infection were asked to stay home, received testing and were managed by the Occupational Health and Safety Division.

All patients admitted without SARS-CoV-2 infection with high levels of exposure to a person positive for SARS-CoV-2 infection were prospectively flagged by IPAC as close contacts and followed a 14-day quarantine under droplet and contact precautions, with daily symptom monitoring and, from late April 2020, repeated PCR testing. When COVID-19 outbreaks occurred on wards, additional measures were initiated: high-touch surface disinfection, restricted patient transfers, implementation of droplet and contact precautions for all patients, and SARS-CoV-2 PCR testing if symptoms developed, and from Apr. 21, repeated testing of all patients even if asymptomatic.





Outcomes

The primary clinical outcome was in-hospital mortality. Secondary clinical outcomes were dispositions at discharge, and hospital readmission rates up to 90 days after discharge. Additionally, we looked at the prevalence of patients with HASARS-CoV-2 infection and acquisition of infection in patients who shared a multi-bed room with patients with known SARS-CoV-2 infection during their period of contagiousness (from 2 d before symptom onset to 10 d after). Acquisition of SARS-CoV-2 infection was linked to viral transmission between patients in the same room only if close contacts developed symptoms (or tested positive if asymptomatic) 3 or more days after symptom onset in the index patient and their first contact, and up to 14 days after their last contact. We used a 3-day gap as it represents the lower end of the SARS-CoV-2 serial interval.¹⁵

Statistical analysis

We summarized continuous variables as median with the interquartile range (IQR), and categorical variables as proportions. We compared outcomes between the HA and NHA groups using χ^2 test for categorical data. To evaluate the association between HA-SARS-CoV-2 infection and in-hospital mortality, we performed a multivariable logistic regression by including the following prespecified risk factors for death in patients with SARS-CoV-2: age, sex, moderate to severe chronic renal disease, solid tumour, hematologic malignancy, diabetes, chronic obstructive pulmonary disease (COPD) and myocardial infarction. Considering the potential interaction between age and HA status on mortality, we calculated agegroup-specific odds ratios for HA-SARS-CoV-2 infection.

This was further supported by the presence of interaction on univariate analysis. We quantified the degree of collinearity using variance inflation factors. As a sensitivity analysis, we performed the same analysis for only proven HA cases after excluding all suspected HA cases. We used STATA MP version 16.1 for all analysis.

Ethics approval

The Research Ethics Board of the Centre intégré universitaire de santé et de services sociaux (CIUSSS) de l'Est-de-l'Île-de-Montréal approved our study protocol.

Results

During the 3-month period, 734 patients were screened for inclusion and 37 were excluded, resulting in 697 patients either admitted to hospital with COVID-19 or who had acquired SARS-CoV-2 infection while in hospital (Figure 1). The first admission of a patient with COVID-19 was on Mar. 19, 2020, and the first patient with HA-SARS-CoV-2 infection became symptomatic on Mar. 24 (epidemic curve shown in Figure 2). A total of 253 (36.3%) patients with HA-SARS-CoV-2 infection were classified as being HA (proven: 217 [85.4%]; suspected: 36 [14.6%]). Among patients with proven HA-SARS-CoV-2, 101 (46.5%) had a positive SARS-CoV-2 PCR test more than 14 days after admission; the 116 others had an epidemiologic link identified (see Appendix 1, eFigure 1, for timing of diagnosis from admission day). Out of 139 identified close-contact patients associated with sharing a multi-bed room with a patient with COVID-19, 45 (32.4%) developed

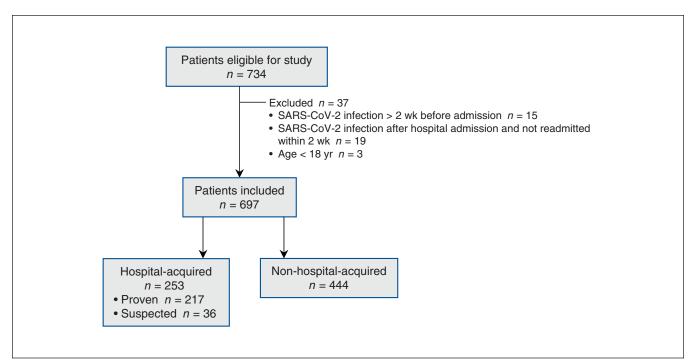


Figure 1: Flow chart of included patients with SARS-CoV-2 infection in hospital.



SARS-CoV-2 infection while in hospital, and 6 had a positive SARS-CoV-2 PCR test with an unknown date of symptom onset within 14 days after discharge (3 within 7 d). We classified 444 patients as NHA, comprising 406 (91.2%) community-acquired cases.

The median age was 75 years (IQR 62-85) for the full cohort and 356 (51.1%) patients were female (Table 1). Age younger than 75 years was less frequent in the HA group (n = 98 [38.7%], p = 0.003) than in the NHA group (n = 231)[52.0%]). Patients with HA-SARS-CoV-2 infection had a higher previous 5-year history of cancer (localized n = 49[19.4%], HA group v. n = 39 [8.8%], NHA group; metastatic n = 28 [11.1%], HA group v. n = 14 [3.2%], NHA group; p < 0.001) and COPD (n = 60 [23.7%], HA group v. n = 65 [14.6%], NHA group; p = 0.003). Surgical procedures were performed more frequently in patients with HA-SARS-CoV-2 infection than in patients with NHA infection (n = 37 [14.6%] v. n = 13 [2.9%]; p = 0.001). Corticosteroid treatment was prescribed in 46 (18.2%) patients with HA infection and 66 (14.9%) patients with NHA infection (p = 0.25). Two patients with HA-SARS-CoV-2 infection received tocilizumab and 3 patients with NHA infection received hydroxychloroguine. Both treatments were not recommended for COVID-19 at the time of our study.

Clinical outcomes

Patients with HA-SARS-CoV-2 infection had a higher rate of in-hospital mortality ((n = 99 [39.1%])) than patients with NHA infection (n = 115 [25.9%], p = 0.001), with lower rates of ICU admission and requirement for mechanical ventilation (n = 21 [8.3%] v. n = 85 [19.1%], p < 0.001 and n = 9[3.6%] v. n = 58 [13.0%], p = 0.001, respectively) (Table 2). Most patients with SARS-CoV-2 infection in the ICU admitted within 7 days of a positive test (n = 17 [81.0%] in the HA group v. n = 74 [87.1%] in the NHA group, p =0.47). Patients who were discharged after HA-SARS-CoV-2 infection were less likely to be discharged directly home and were more likely to be transferred to a rehabilitation centre than patients with NHA infection (p = 0.001). Readmissions within 90 days after discharge occurred more frequently in the HA group than in the NHA group (n = 24 [15.3%] v.n = 13 [4.0%], p = 0.001).

After multivariable analysis, patients younger than 75 years with HA-SARS-CoV-2 infection had increased odds of death over patients with NHA infection in hospital (odds ratio [OR] 2.78, 95% confidence interval [CI] 1.44–5.38) (Table 3). There was no increased risk of death for older patients (OR 1.25, 95% CI 0.64–2.42 in the 75–84-yr age group and OR 0.75, 95% CI 0.41–1.35 in the ≥ 85-yr age group) compared with patients younger than 75 years. Moderate to severe

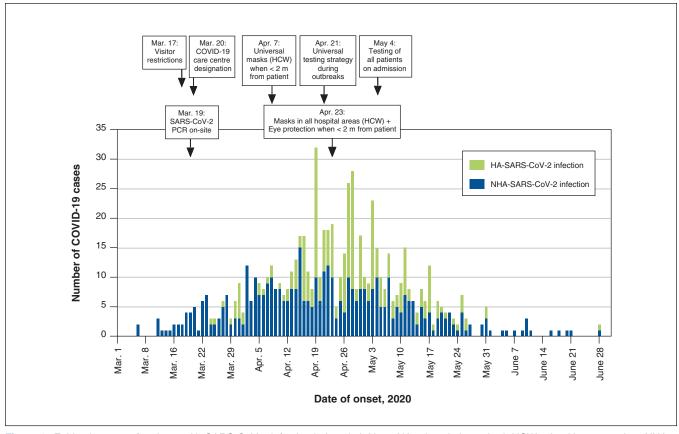


Figure 2: Epidemic curve of patients with SARS-CoV-2 infection in hospital. Note: HA = hospital-acquired, HCW = health care worker, NHA = non-hospital-acquired, PCR = polymerase chain reaction.



	No. (%)* of hospital- acquired cases	No. (%)* of non-hospital- acquired cases	
Characteristic	n = 253 (36.3%)	n = 444 (63.7%)	p value
Age, yr, median (IQR)	79 (68–86)	73 (58.5–85)	
Age, yr			0.003
< 75	98 (38.7)	231 (52.0)	
75–84	71 (28.1)	100 (22.5)	
≥ 85	84 (33.2)	113 (25.5)	
Female sex	128 (50.6)	228 (51.4)	0.85
Comorbidity†			
Moderate to severe chronic kidney disease‡	35 (13.8)	52 (11.7)	0.42
Solid tumour			< 0.001
Localized	49 (19.4)	39 (8.8)	
Metastatic	28 (11.1)	14 (3.2)	
Hematologic malignancy	12 (4.7)	10 (2.3)	0.07
Diabetes	87 (34.4)	156 (35.1)	0.84
COPD	60 (23.7)	65 (14.6)	0.003
Myocardial infarction	18 (7.1)	33 (7.4)	0.91
Dementia	58 (22.9)	101 (22.8)	0.96
Charlson Comorbidity Index, median (IQR)	2 (1–4)	1 (0–3)	
Provenance before admission§			< 0.001
Home	180 (71.2)	237 (53.4)	
Long-term care facility	9 (3.6)	49 (11.0)	
Others	62 (24.4)	160 (36.1)	
Reason for admission			< 0.001
Infectious	70 (27.9)	7 (1.6)	
Nervous system	38 (15.1)	7 (1.6)	
Neoplasm	37 (14.7)	4 (0.9)	
Gastrointestinal	21 (8.4)	9 (2.0)	
Other	85 (33.9)	419 (93.9)	
Deprivation index of 4 or 5¶	150 (59.3)	243 (54.7)	0.16
Timing of diagnosis, d			< 0.001
0–6	62 (24.5)	444 (100)	
7–14	91 (36.0)	0 (0)	
> 14	100 (39.5)	0 (0)	
Treatment with corticosteroids	46 (18.2)	66 (14.9)	0.25
Surgical procedure	37 (14.6)	13 (2.9)	0.001
ICU admission	21 (8.3)	85 (19.1)	< 0.001
ICU admission within 7 days	17 (81.0)	74 (87.1)	0.47
Mechanical ventilation	9 (3.6)	58 (13.0)	0.001

Note: COPD = chronic obstructive pulmonary disease, ICU = intensive care unit, IQR = interquartile range, RPA = Résidence privée pour ainés (private residences for older adults).

^{*}Unless stated otherwise.

[†]Selected comorbidities from the Charlson Comorbidity Index. 12

[‡]Moderate to severe chronic renal disease, defined as creatinine > 265 µmol/L, as defined in the Charlson Comorbidity Index.¹²

[§]Others: congregate living settings such as RPA, intermediate and family-type resources (IR-FTR), transfer from another hospital and rehabilitation.

¶The deprivation index is based on patient postal code and 2016 census data. Results of various indicators are aggregated to create a deprivation index to

[¶]The deprivation index is based on patient postal code and 2016 census data. Results of various indicators are aggregated to create a deprivation index to identify a deprived population. A score from 1 (least deprived) to 5 (most deprived) is calculated, with 4 and 5 signifying being deprived and most deprived.¹¹



Table 2: Outcomes in patient with hospital-	2: Outcomes in patient with hospital-acquired and non-hospital-acquired SARS-CoV-2 infection			
Outcomes	No. (%)* of hospital- acquired cases n = 253 (36.3%)	No. (%)* of non- hospital-acquired cases n = 444 (63.7%)	<i>p</i> value	
Mortality by age, yr	99 (39.1)	115 (25.9)	0.001	
< 75	29 (29.6)	23 (10.0)		
75–84	33 (46.5)	37 (37.0)		
≥ 85	37 (44.1)	55 (48.7)		
Hospital length of stay, median (IQR)	25.0 (15–46)	8 (3.5–16)		
Disposition at discharge†			0.001	
Home	74 (48.1)	197 (59.9)		
Long-term care facility	32 (20.8)	73 (22.2)		
Rehabilitation	26 (16.9)	20 (6.1)		
Others‡	22 (14.3)	39 (11.9)		
Readmission within 90 days after discharge	24 (15.3)	13 (4.0)	0.001	

Note: IQR = interquartile range, RPA = Résidence privée pour ainés (private residences for older adults).

*Unless stated otherwise.

chronic renal disease, solid metastatic cancer and hematologic malignancy were all associated with an increased odds of death. Conversely, being female seemed protective (OR 0.60, 95% CI 0.42–0.87). In the sensitivity analysis after excluding suspected HA cases, HA-SARS-CoV-2 infection status remained a significant risk factor for mortality (Appendix 1, eTable 2). No significant collinearity was detected between our covariates.

Interpretation

In the present study, one-third of all cases of SARS-CoV-2 infection in patients in hospital were acquired owing to inhospital transmission, with a higher mortality rate among patients younger than 75 years. Similar data from England reported that about 25% of COVID-19 cases in hospital were acquired during the hospital stay.¹⁶

A major factor influencing the prevalence of HA-SARS-CoV-2 infection is the hospital's infrastructure. Most of our wards have no mechanical ventilation systems and 2- and 4-bed rooms are separated by curtains. This design explains why one-third of patients sharing a room with a patient with COVID-19 subsequently tested positive for SARS-CoV-2 infection, even before the emergence of more contagious variants of concern. This proportion is consistent with household transmission rates between spouses (37.8%, 95% CI 25.8%–50.5%)¹⁷ and other reports on transmission between hospital roommates (up to 39%).^{18,19}

Although only 45/254 (17.7%) of cases of HA-SARS-CoV-2 infection in our study were directly linked to transmission between patients in a multi-bed room, more HA cases

	Table 3: Multivariable logistic regression of factors associated with mortality related to SARS-CoV-2 infection		
	Factors	OR (95% CI)	

Factors	OR (95% CI)
HA cases, age, yr*	
< 75	2.78 (1.44–5.38)
75–84	1.25 (0.64–2.42)
≥ 85	0.75 (0.41-1.35)
Sex	
Female	0.60 (0.42-0.87)
Solid tumour†	
Localized	1.07 (0.63-1.80)
Metastatic	5.91 (2.84–12.30)
Hematologic malignancy	6.66 (2.41–18.4)
Moderate to severe chronic renal disease‡	2.96 (1.74-5.04)
Diabetes	1.20 (0.81–1.76)
Chronic obstructive pulmonary disease	1.02 (0.64–1.62)
Myocardial infarction	0.90 (0.47–1.74)

Note: CI = confidence interval, HA = hospital-acquired, OR = odds ratio, Ref. = reference

*Ref. = non-HA cases.

†Ref. = y.

‡Defined as creatinine > 265 µmol/L

might be indirectly linked to high population density.⁷ The importance of crowding on COVID-19 incidence and mortality has already been shown in Canadian long-term care settings.²⁰ Although difficult to quantify, various shortages (e.g.,

[†]Disposition at discharge was calculated only for survivors (n = 154 in hospital-acquired group and n = 329 in non-hospital-acquired group). ‡Others: congregate living settings such as RPA, intermediate and family-type resources (IR-FTR) and transfer to another hospital or dedicated centres for quarantine of patients with COVID-19.





medical masks, PPE, hand sanitizer) might also have affected transmission rates.^{21,22} Nonetheless, as shown by Brigham and Women's Hospital's first-wave experience in Boston, Massachusetts, under optimal conditions, in-hospital transmission can be limited: only 1 case of COVID-19 was deemed to be hospital acquired among 697 hospital admissions.²³ With new variants being of concern for increased transmissibility and potentially increased risk of death, it is even more important to reinforce nonpharmaceutical interventions to prevent nosocomial SARS-CoV-2 transmission.^{24,25}

The mortality rate of patients with HA-SARS-CoV-2 infection in our study is also similar to that in existing data in the literature. ^{4,7} Our NHA-SARS-CoV-2 infection group provided a good representation of patients with most severe HA-COVID-19, with 91.2% of the total NHA cases being community acquired and a mortality rate of 26.4%. Nonetheless, patients with HA-SARS-CoV-2 infection still had a higher mortality rate. In a cohort study of 252 patients in hospital with active cancer and COVID-19, HA-COVID-19 was an independent risk factor of mortality (hazard ratio [HR] 2.3, 95% CI 1.3–4; p = 0.005). The mortality rate of that study's HA-COVID-19 group was higher than in our results (47% v. 38%), likely because their cohort comprised exclusively patients with cancer.

Similarly, a history of metastatic cancer and hematologic malignancies were independent risk factors for death in our study. Therefore, the seriousness of the admission pathology has an important impact on patient outcome. A patient in hospital already weakened by an acute illness will have a difficult time managing the added physiologic stress of HA-SARS-CoV-2 infection. In another cohort study, HA-COVID-19 was not a risk factor for death compared with NHA-COVID-19 (HR 0.71, 95% CI 0.51-0.98).8 However, these authors did not stratify for age. The estimated risk of death for COVID-19 in adults aged 80 years and older in hospital is 60% irrespective of modes of acquisition.²⁷ In our study, the increased risk of death from the inhospital acquisition of SARS-CoV-2 infection seemed to decrease with increasing age. This can be explained by an increase in comorbidities and frailty overwhelming the potential increased risk from HA-SARS-CoV-2 infections for older patients.

Limitations

There are limitations to our study. First, it is a single-centre retrospective study, which limits the generalizability of our transmission data and is also not meant to prove causality. Second, SARS-CoV-2 PCR testing capacity and indications changed quickly throughout the pandemic, potentially underestimating the prevalence of asymptomatic and paucisymptomatic cases of HA-SARS-CoV-2 infection. Third, there was no systematic postdischarge follow-up to assess whether patients developed COVID-19 after potential inhospital exposure, possibly underestimating HA-COVID-19 cases and SARS-CoV-2 infection by close contacts. Fourth, while our objective was to show the added mortality of concomitant illness on patients with SARS-CoV-2 infection,

other potential confoundings associated with our classification might not be adequately adjusted by our regression model, possibly resulting in overestimation of the effect size. Also, lack of inter-rater reliability on data collection should be taken into consideration. Finally, combining proven and suspected cases might bias our results toward the null, therefore strengthening the positive results found in patients younger than 75 years.

Conclusion

For patients younger than 75 years, acquisition of SARS-CoV-2 infection in hospital resulted in a higher risk of death than acquisition outside of hospital. Patients in hospital are vulnerable and at increased risk of complications if exposed to SARS-CoV-2. In-hospital viral transmission remains a major concern for patients, as many hospital design features are challenging to correct and circulating variants of SARS-CoV-2 now seem more contagious. Even in the face of pandemic fatigue, these findings justify taking extraordinary measures to prevent COVID-19 hospital transmission and avoid preventable death.

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