Characteristics and treatment differences in hospitalized older adults with COVID-19 during waves 1 and 2: a multicentre case series

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Abstract

The first and second waves of COVID-19 infections in Ontario, Canada, were marked by differences in patient characteristics and treatment. Our objectives were to compare (i) patient characteristics, treatment and outcomes of hospitalized older adults with COVID-19 between waves 1 and 2, and (ii) patient characteristics and outcomes in those receiving dexamethasone, remdesivir and tocilizumab during wave 2.

Methods

We completed this case series in seven hospitals in Toronto, Canada. Hospitalized older adults aged ≥65 years with confirmed COVID-19 infection were included. Wave 1 extended from March 11 to July 31, 2020 and wave 2 from August 1, 2020 to April 30, 2021. Patient characteristics and outcomes were abstracted from charts and analyzed descriptively. A multivariable model was used to determine the association of dexamethasone and delirium.

Results

In acute care hospitals, 296 patients were admitted in wave 1 and 631 patients in wave 2. Patients were older in wave 2 than in wave 1 (median age 80.0 vs. 78.0 years, p=0.016) but frailty was similar. There was increased use of dexamethasone in wave 2, but it was not independently associated with delirium incidence (adjusted odds ratio 1.18, 95% confidence interval 0.73–1.95). There were no differences in mortality, delirium, ICU admissions or complications between waves. Length of stay was reduced by 3 days in wave 2 (median 10.0 vs. 13.0 days in wave 1, p=0.034).

Interpretation

Despite better treatment, outcomes in hospitalized older adults with COVID-19 were similar between the two waves except for shorter length of stay.

Characteristics and treatment differences in hospitalized older adults with COVID-19 during waves 1 and 2: a multicentre case series

Introduction

The COVID-19 pandemic was marked by multiple waves as the infection waxed and waned. The waves of COVID-19 infection in Ontario, Canada were due to seasonality [1], changes in public health measures [2], and the emergence of new COVID-19 strains [3]. Little was known about the treatment of COVID-19 during the first wave of hospitalizations, which predominantly affected older adults [4]. When the second wave started on August 1, 2020 [5], there was more familiarity with isolation measures and more treatments available, but concerns remained about hospital capacity during the winter [6]. Wave 2 led to over 10 times more cases than wave 1 [7].

While the virus was evolving, vaccines and therapeutic drugs were rapidly developed worldwide [8]. Vaccination of long-term care (LTC) residents in Ontario led to a dramatic reduction of infections [9], but most community-dwelling older adults were vaccinated at the end of wave 2 [10]. As a result, older adults continued to be infected and hospitalized in wave 2. Fortunately, new therapies were found to be effective for treatment of hospitalized COVID-19 patients, including dexamethasone [11], remdesivir [12] and tocilizumab [13]. The use of dexamethasone led to concerns of increased delirium risk in older adults [14].

Given the differences in disease characteristics and treatment strategies between the two waves, we wanted to assess outcome differences in hospitalized older adults with COVID-19. Our objectives were to compare (i) differences in patient characteristics, treatment and outcomes of hospitalized older adults with COVID-19 between waves 1 and 2, and (ii) patient characteristics and outcomes in those receiving dexamethasone, remdesivir and tocilizumab during wave 2.

Methods

This multicentre case series included patients admitted to seven hospitals in Toronto, Canada from March 11, 2020 to April 30, 2021. Five hospitals admitted acute care patients (Mount Sinai Hospital, St. Michael's Hospital, Sunnybrook Health Sciences Centre, Toronto General Hospital, and Toronto Western Hospital). Two hospitals admitted rehabilitation and LTC residents (Baycrest Health Sciences and Providence Healthcare). Wave 1 of the pandemic occurred from March 11, 2020 to July 31, 2020. Wave 2 cases were included from August 1, 2020 to April 30, 2021 [15]. Research ethics approval was obtained through Clinical Trials Ontario (3186-OPIA-Apr/2020-38044).

Inclusion criteria

1. Patients with COVID-19 infection confirmed by viral polymerase chain reaction (PCR) swab available on hospital health records.
2. Age ≥65 years when COVID-19 detected.

Exclusion criteria

1. Re-admission to hospital after index admission for COVID-19. Only records from the initial admission were included.
2. False positive swab as defined by the infection control or treatment team assessment and removal of isolation precautions.
3. Recovered COVID-19 infection as defined by infection control or treatment team assessment and removal of isolation precautions.

We only included the acute care admission if patients were diagnosed with COVID-19 at a rehabilitation or LTC home but later transferred to acute care for COVID-19. If patients were diagnosed with COVID-19 in acute care and later transferred to rehabilitation or LTC home, we only included the acute care stay.

Data collection and processing

Patients meeting inclusion criteria were identified by decision support at each site. A trained chart assessor abstracted data using case report forms hosted on a REDCap database. Each chart assessor was trained by a physician investigator at the hospital site (BL, JW, EW, KP, TI, and AV). The first five charts were extracted in duplicate with the physician investigator, and the physician investigator reviewed additional charts when the chart assessor had questions.

Missing or erroneous data (e.g. dates that were outside of the study range or temperatures that were outside of physiologic range) were reviewed by the site physician investigator. Missing CFS was imputed as 6 (severe frailty) for LTC residents and 5 (moderate frailty) for retirement home residents based on local LTC admission criteria and published frailty estimates [16,17].

A protocol is available on Open Science Framework (https://osf.io/k4g7a/). Please see Supplementary appendix 1 for details of data collection and processing.

Analysis

The acute care and rehabilitation/LTC patients were analysed separately. Patient characteristics and outcomes were analysed descriptively with counts (proportions), means (standard deviation) and medians (interquartile range), where appropriate. Statistical tests were used to compare data, including chi-squared test (categorical variables), ANOVA test (continuous variables), and Kruskal-Wallis test (non-normal variables). A multivariable logistic

regression model was used to identify the independent association of dexamethasone use with delirium. Missing data in the model were handled by listwise deletion. Statistical significance was defined at $p<0.05$. Model variables were tested for multicollinearity, fit was tested using the Hosmer-Lemeshow test and discrimination was tested using the c-statistic. The analysis was done in R version 4.0.3 [18].

Reporting standard

The Consensus-based Clinical Case Reporting Guideline (CARE) was used for reporting this case series [19].

Results

Acute care hospitals

In the 927 patients admitted to an acute care hospital during both waves (Table 1), the median age was 79.0 years (interquartile range, IQR, 72.0–78.0) and 417 (45.0%) were female. Compared to the first COVID-19 wave (n=296), patients admitted in wave 2 (n=631) were older (median age 80.0 vs. 78.0 years, p=0.016) and fewer were from LTC (15.7% vs. 25.3%, p=0.001). There were no differences in the proportion with impairment in activities of daily living. A similar proportion of patients were frail as defined by CFS ≥5 in both waves (61.9% vs. 61.9%).

In the acute care cohort during both waves, dementia was present in 212 patients (23.1%) and 132 had a history of falls (14.3%). Baseline comorbidities were not significantly different between waves 1 and 2 except for fewer patients with a history of falls (12.4% vs. 18.3%, p=0.023) and strokes (16.4% vs. 22.9%, p=0.024) in wave 2. A larger proportion of patients

indicated full resuscitation at baseline in wave 2 (58.5% vs. 49.6%, p=0.001) and a smaller proportion indicated do not resuscitate in wave 2 (38.2% vs. 42.5%). On presentation, more patients had an infiltrate on chest x-ray in wave 2 (73.6% vs. 66.3%, p=0.030).

Treatment and outcome differences in waves 1 and 2

Significantly more patients received dexamethasone (71.5% vs. 3.0% , p<0.001), remdesivir (15.7% vs. 0%, p<0.001), and tocilizumab (3.8% vs. 0.3%, p=0.005) in wave 2 than wave 1. No patients received hydroxychloroquine and lopinavir/ritonavir in wave 2. More patients were enrolled in clinical trials in wave 2 (11.7% vs. 5.1% in wave 1, p=0.003).

There was no difference in the proportion of in-hospital deaths between the two waves (28.9% in wave 2 vs. 27.3% in wave 1, p=0.693). Delirium prevalence, delirium incidence, hospital complications and ICU admissions were similar between waves 1 and 2 (Table 2). The median length of stay was reduced in wave 2 (10.0 days [IQR 6.0–19.0] vs. 13.0 days [IQR 5.0–25.3], p=0.034).

Delirium characteristics between waves 1 and 2

Patients with delirium in wave 2 were older (median age 84.0, IQR 74.0–90.0, vs. 80.0, IQR 74.0–87.0, p=0.005), and more likely to have delirium onset in hospital (32.5% vs. 21.3% in wave 1, p<0.001). Agitation was more common in wave 2 (61.4% vs. 48.5% in wave 1, p=0.008). There were more in-person essential care visitors in wave 2 (23.5% vs. 14.7% in wave 1, p=0.035).

Characteristics and outcomes associated with the use of dexamethasone, remdesivir and tocilizumab in wave 2

We analyzed patient characteristics and outcomes associated with the use of dexamethasone, remdesivir and tocilizumab only in the wave 2 cohort (Table 4). Patients who received dexamethasone had similar age, frailty and cognitive status as those who did not get the drug. Fewer females received drug treatment (42.9% vs. 54.4%, p=0.011). Patients who received dexamethasone were more likely to have a fever (53.0% vs. 33.3%) and had higher mean CRP levels (109.32 vs. 45.15mg/L). Dexamethasone use was associated with higher in-hospital mortality (37.3% vs. 7.4%, p<0.001), longer length of stay (11.0 vs. 7.0 days, p<0.001), increased ICU admissions (28.6% vs. 11.3%, <0.001), increased delirium prevalence (59.2% vs. 37.9%, p<0.001) and increased restraint use (24.2% vs. 9.4%, p<0.001). In a supplementary analysis using the entire cohort (waves 1 and 2), dexamethasone had a similar association with these outcomes (Supplementary table 1). Remdesivir and tocilizumab were not associated with differences in mortality, length of stay, delirium, or restraint use in wave 2. However, both drugs were given to younger, less frail patients with fewer comorbidities (Table 4).

Dexamethasone and delirium in wave 2

Although dexamethasone was associated with increased delirium prevalence, the association with delirium incidence was not statistically significant (22.9% vs. 16.6%, p=0.103). In a multivariable model (Supplementary table 2), dexamethasone use was not associated with delirium incidence in wave 2 (adjusted odds ratio, aOR, 1.18, 95% CI 0.73–1.95) after adjusting for age (aOR 1.14 for every 5 years increase, 95% CI 1.01–1.29), dementia (aOR 1.40, 95% CI

0.84–2.33), ICU admission (aOR 3.11, 95% CI 1.93–5.02), and clinical frailty scale (1.12, 95% CI 0.95–1.34).

Rehabilitation hospitals and LTC homes

In the two facilities that provided rehabilitation and LTC services, there were 19 patients in wave 1 and 96 patients in wave 2 (Supplementary table 3). At baseline, patients in these facilities were older compared with those in acute care (median age 86.0 vs. 79.0 in acute care, p<0.001) and there was a higher proportion of females (62.6% vs. 45.0% in acute care, p=0.001). They were also more frail and more likely to have dementia and falls (Supplementary table 3). Comparing between the two waves, there were no significant differences in characteristics or outcomes. The proportion of deaths were smaller in wave 2, but this was not statistically significant (21.9% vs. 36.8% in wave 1, p=0.273). The main difference in treatment was the administration of dexamethasone in these facilities during wave 2 (26.0% vs. 0% in wave 1, p=0.027). Dexamethasone was used in 7 patients (13.2%) in LTC and in 18 patients (41.9%) in rehabilitation setting. The prevalence of delirium was low (15.8% in wave 1 and 14.6% in wave 2, p=0.998) and there was no documented restraint use in both waves.

Discussion

This multicentre case series of older patients admitted to hospital with COVID-19 highlighted differences in the patient population, treatment and outcomes between waves 1 and 2 of the pandemic. To our knowledge, this is the first study comparing the characteristics of older adults admitted with COVID-19 between the first two waves of the pandemic in Canada. The proportion of in-hospital deaths, delirium and complications were similar between the two waves

despite more effective and available drugs. This finding is in agreement with published studies comparing survival of ICU patients in waves 1 and 2 in Europe, where an improvement in survival was not seen [20,21]. In our study, the length of stay was reduced in wave 2, which was not a reported benefit in the randomized trials of corticosteroids in COVID-19 [11].

Complicating wave 2 of the pandemic was the rise of SARS-CoV-2 variants [22]. In Ontario, Canada, the prevalence of variants increased from 15% of all cases in early February 2021 to nearly 90% in April 2021 [7]. Variant data was not captured in our study because researchers were not allowed to access the external health portal where variant sequencing results were hosted. Given the rise of variants in the province, we assumed that most patients in wave 2 were infected with a variant. The increased virulence of the variants [22] may explain the lack of improvement in mortality in the second wave, despite the prevalent use of disease modifying drugs (e.g. 71% on dexamethasone). Another explanation for the lack of mortality improvement in wave 2 may be related to the efficacy of the drugs in older adults. A systematic review of steroid trials in COVID-19 patients showed that the median age of trial participants ranged from 57–67, with few patients aged >80 years [11]. In contrast, the median age in our wave 2 cohort was 80 years (IQR 72–88). In the absence of randomized data, an observational study in France (n=267) showed improved survival for patients age >80 years on corticosteroids (hazard ratio 0.67, 95% confidence interval 0.46–0.99). This study was done between March and April 2020, when the wild type strain was circulating. The benefits were potentially attenuated with the variants.

Our study revealed a 3-day reduction in length of stay during wave 2 in acute care patients. Canadian data from January to November 2020 demonstrated a mean length of stay of 15 days. Wave 2 was associated with an increase in ICU length of stay in Ontario, but the

majority of admitted patients were between ages 40–79 years [23]. The reduction in length of stay may be reflective of better recovery time in non-ICU patients with the use of effective drugs. Trials and observational studies of corticosteroids have not reported a reduction in length of stay [11,24], but remdesivir was shown to improve time to recovery [12]. However, only 15.7% of patients received remdesivir in our study, suggesting that other medications (e.g. steroids or tocilizumab [13]) or interventions (e.g. proning [25]) likely played an important role. Perhaps dexamethasone was more effective in a subgroup of older adults who were less sick, which shortened time to discharge. We found that remdesivir and tocilizumab were given preferentially to younger, less frail patients, which may indicate inequity in the distribution of therapeutic medications.

Steroid use has been reported to increase delirium risk in the ICU literature [26]. Our data showed that dexamethasone use was associated with increased delirium prevalence but not incidence. The strength of the association with delirium incidence was reduced after adjusting for covariates. Our data suggest that dexamethasone use was not independently associated with increased delirium risk, but patients who received dexamethasone likely had increased disease severity, which was associated with delirium. It is possible that dexamethasone was associated with increased delirium severity, but this was not assessed in our study. There was a 2.6-fold increase in physical restraint use in patients given dexamethasone, which may suggest increased delirium severity [27].

There are some limitations to our data. First, we used a retrospective design, so we could not prospectively collect frailty, delirium, and functional status data. Second, we did not capture COVID-19 variants because not all hospitals had access to public health variant sequencing results. Third, we did not ascertain whether delirium onset occurred before or after

dexamethasone use because the study was designed before there was widespread dexamethasone use. Fourth, we did not assess the dosages or clinical context when COVID-19 drugs were given. Fifth, we did not collect other demographic characteristics such as gender, race, language, and socioeconomic status.

There are several strengths to our study. It was large and included hospitalized older adults since the beginning of the pandemic in multiple hospitals in Toronto, Canada. Every acute care hospital used an electronic medical record system where pertinent data were readily available.

Conclusion

Despite better therapeutic drugs, older adults hospitalized with COVID-19 did not have improved mortality or delirium risk in the second wave, but length of stay was shorter. Future research should explore ways to improve the outcomes of hospitalized older adults during pandemics.

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Table 1: Baseline characteristics of older adults aged ≥65 admitted to acute care hospital with COVID-19 in waves 1 and 2.

	Cohort	Wave 1	Wave 2	p-value
n (%)	927 (100)	296 (31.9)	631 (68.1)	
Age, median (IQR)	79.0 (72.0–87.0)	78.0 (71.0–85.0)	80.0 (72.0–88.0)	0.016
Female, n (%)	417 (45.0)	126 (42.6)	291 (46.2)	0.336
From long-term care, n (%)	174 (18.8)	75 (25.3)	99 (15.7)	0.001
Any impairment in activities of daily living, n (%)	359 (38.7)	110 (37.2)	249 (39.5)	0.550
Any impairment in instrumental activities of daily living, n (%)	497 (53.6)	137 (46.3)	360 (57.1)	0.003
Clinical frailty scale, mean (SD)	4.95 (1.55)	5.10 (1.61)	4.88 (1.51)	0.053
Frail (CFS ≥5), n (%)	552 (61.9)	174 (61.9)	378 (61.9)	1
Baseline mobility, n (%)				<0.001
Walks independently	371 (41.0)	91 (31.6)	280 (45.4)	
Walks with cane	56 (6.2)	19 (6.6)	37 (6.0)	
Walks with walker	245 (27.1)	78 (27.1)	167 (27.1)	
Wheelchair	90 (9.9)	32 (11.1)	58 (9.4)	
Bedbound	44 (4.9)	15 (5.2)	29 (4.7)	
Undocumented	99 (10.9)	53 (18.4)	46 (7.5)	
Baseline code status, n (%)				0.001
Full code	463 (55.6)	132 (49.6)	331 (58.5)	
Do not resuscitate	329 (39.5)	113 (42.5)	216 (38.2)	
Only intubation	21 (2.5)	13 (4.9)	8 (1.4)	
Other option	8 (1.0)	6 (2.3)	2 (0.4)	
Undocumented	11 (1.3)	2 (0.8)	9 (1.6)	
Comorbidities, n (%)				
Dementia	212 (23.1)	64 (21.8)	148 (23.8)	0.560
Falls	132 (14.3)	54 (18.3)	78 (12.4)	0.023
Heart failure	131 (14.2)	48 (16.3)	83 (13.2)	0.250
Coronary artery disease	220 (23.9)	78 (26.5)	142 (22.6)	0.228
Chronic kidney disease	189 (20.5)	62 (21.1)	127 (20.2)	0.829
Stroke	170 (18.5)	67 (22.9)	103 (16.4)	0.024
Hypertension	637 (69.0)	212 (71.9)	425 (67.7)	0.227
Diabetes	369 (40.0)	125 (42.5)	244 (38.9)	0.324
Chronic obstructive pulmonary disease	112 (12.2)	43 (14.6)	69 (11.0)	0.147
Cancer	217 (23.6)	65 (22.2)	152 (24.2)	0.547
Presenting characteristics				
Any infiltrate on chest x-ray, n (%)	632 (71.3)	191 (66.3)	441 (73.6)	0.030
Maximum temperature (ºC) on presentation, median (IQR)	37.7 (37.0–38.4)	37.9 (37.0–38.7)	37.6 (37.0–38.4)	0.050
Days from prodromal symptoms to COVID-19 diagnosis, median (IQR)	3.0 (1.0–7.0)	4.0 (1.8–7.0)	3.0 (0.5–7.0)	0.004

IQR = interquartile range; SD = standard deviation; CFS = clinical frailty scale.

Table 2: Outcomes and treatment of older adults aged ≥65 admitted to acute care hospital with COVID-19 in waves 1 and 2.

	Cohort	Wave 1	Wave 2	p-value
n (%)	927 (100)	296 (31.9)	631 (68.1)	
COVID-19 treatment, n (%)				
Dexamethasone	460 (49.6)	9 (3.0)	451 (71.5)	<0.001
Azithromycin	203 (21.9)	70 (23.6)	133 (21.1)	0.425
Remdesivir	99 (10.7)	0 (0.0)	99 (15.7)	<0.001
Other steroid	56 (6.0)	21 (7.1)	35 (5.5)	0.439
Tocilizumab	25 (2.7)	1 (0.3)	24 (3.8)	0.005
Convalescent plasma	18 (1.9)	1 (0.3)	17 (2.7)	0.03
Lopinavir/ritonavir	6 (0.6)	6 (2.0)	0 (0.0)	0.002
Hydroxychloroquine	4 (0.4)	4 (1.4)	0 (0.0)	0.017
Participation in clinical trial, n (%)	80 (9.2)	15 (5.1)	56 (11.7)	0.003
Surgery in hospital, n (%)	44 (5.0)	19 (6.4)	24 (5.0)	0.496
Outcomes				
In-hospital death, n (%)	262 (28.4)	81 (27.4)	181 (28.9)	0.693
Length of stay, median (IQR)	11.0 (6.0–22.0)	13.0 (5.0–25.3)	10.0 (6.0–19.0)	0.034
Delirium prevalence, n (%)	497 (54.1)	165 (55.7)	332 (53.3)	0.531
Delirium incidence, n (%)	201 (21.8)	69 (23.3)	132 (21.1)	0.505
ICU admission, n (%)	215 (23.4)	67 (22.8)	148 (23.7)	0.831
Any complications, n (%)	432 (46.6)	135 (45.6)	297 (47.1)	0.730
Complications, n (%)				
Physical restraint use	189 (20.4)	63 (21.3)	126 (20.0)	0.707
Respiratory failure	154 (16.6)	43 (14.5)	111 (17.6)	0.283
Acute respiratory distress syndrome	101 (10.9)	25 (8.4)	76 (12.0)	0.127
Other infection	68 (7.3)	19 (6.4)	49 (7.8)	0.550
Aspiration	59 (6.4)	14 (4.7)	45 (7.1)	0.210
Hospital-acquired pneumonia	45 (4.9)	20 (6.8)	25 (4.0)	0.093
In-hospital fall	45 (4.9)	11 (3.7)	34 (5.4)	0.347
Stroke	22 (2.4)	11 (3.7)	11 (1.7)	0.108
Pulmonary embolism	20 (2.2)	4 (1.4)	16 (2.5)	0.360
Heart failure	19 (2.0)	7 (2.4)	12 (1.9)	0.829
Myocardial infarction	18 (1.9)	7 (2.4)	11 (1.7)	0.701
Deep venous thrombosis	9 (1.0)	3 (1.0)	6 (1.0)	1

ICU = intensive care unit.

Table 3: Delirium characteristics of older adults aged ≥65 admitted to acute care hospital with COVID-19 in waves 1 and 2.

	Cohort	Wave 1	Wave 2	p-value
n (%)	497 (100)	165 (33.2)	332 (66.8)	
Age, median (IQR)	82.0 (74.0–89.0)	80.0 (74.0–87.0)	84.0 (74.0–90.0)	0.005
Female, n (%)	220 (44.3)	74 (44.8)	146 (44.0)	0.929
Location of delirium onset, n (%)				<0.001
Home	121 (24.4)	38 (23.2)	83 (25.0)	
Long-term care	110 (22.2)	40 (24.4)	70 (21.1)	
Emergency department	33 (6.7)	15 (9.1)	18 (5.4)	
Ward	143 (28.8)	35 (21.3)	108 (32.5)	
ICU	70 (14.1)	22 (13.4)	48 (14.5)	
Rehabilitation	14 (2.8)	12 (7.3)	2 (0.6)	
Unknown	5 (1.0)	2 (1.2)	3 (0.9)	
History of behavioural and psychological symptoms of dementia, n (%)	110 (22.4)	58 (36.5)	52 (15.7)	<0.001
Motor subtype, n (%)				0.867
Hyperactive	142 (28.9)	43 (26.9)	99 (29.9)	
Hypoactive	182 (37.1)	62 (38.8)	120 (36.3)	
Mixed	83 (16.9)	26 (16.2)	57 (17.2)	
No subtype	84 (17.1)	29 (18.1)	55 (16.6)	
Evidence of agitation, n (%)	283 (57.2)	79 (48.5)	204 (61.4)	0.008
Use of restraints, n (%)	184 (37.0)	63 (38.2)	121 (36.4)	0.780
Use of antipsychotics, n (%)	266 (54.2)	80 (49.7)	186 (56.4)	0.195
Use of any sedating medication, n (%)*	335 (69.5)	104 (65.8)	231 (71.3)	0.263
Use of benzodiazepines, n (%)	154 (31.2)	49 (30.1)	105 (31.8)	0.770
Presence of family or caregivers in person, n (%)	101 (20.7)	23 (14.7)	78 (23.5)	0.035
Use of virtual technology for family or caregivers who could not be present in person, n (%)	278 (57.6)	94 (61.8)	184 (55.6)	0.233

IQR = interquartile range; ICU = intensive care unit.

Table 4: Characteristics and outcomes associated with the use of dexamethasone, remdesivir, and tocilizumab in acute care patients during wave 2.

	No Dexamethasone	Dexamethasone	No remdesivir	Remdesivir	No tocilizumab	Tocilizumab
n (%)	180 (28.5)	451 (71.5)	532 (84.3)	99 (15.7)	607 (96.2)	24 (3.8)
Characteristics						
Age, median (IQR)	79.0 (71.0–86.0)	80.0 (72.0–88.0)	81.0 (72.0–88.0)	75.0 (69.5–84.5)*	80.0 (72.0–88.0)	73.5 (70.0–81.0)*
Female, n (%)	98 (54.4)	193 (42.9)*	253 (47.6)	38 (38.4)	281 (46.4)	10 (41.7)
Frailty†, n (%)	104 (61.2)	274 (62.1)	339 (66.1)	39 (39.8)*	371 (63.0)	7 (31.8)*
Dementia, n (%)	42 (23.6)	106 (23.8)	137 (26.1)	11 (11.1)*	147 (24.5)	1 (4.2)*
CXR infiltrates, n (%)	87 (52.7)	354 (81.6)*	361 (71.5)	80 (85.1)*	425 (73.7)	16 (72.7)
Fever, n (%)	60 (33.3)	239 (53.0)*	242 (45.5)	57 (57.6)*	281 (46.3)	18 (75.0)*
CRP, mean (SD)	45.15 (55.86)	109.32 (81.25)*	94.93 (83.77)	93.51 (70.46)	90.72 (80.17)	150.88 (68.78)*
Outcomes						
In-hospital death, n (%)	13 (7.4)	168 (37.3)*	155 (29.4)	26 (26.3)	172 (28.5)	9 (37.5)
Length of stay, median (IQR)	7.0 (3.0–14.0)	11.0 (7.0–21.0)*	10.0 (5.0–19.0)	11.0 (7.0–22.0)	10.0 (6.0–19.0)	14.0 (7.8–20.0)
Delirium prevalence, n (%)	66 (37.9)	266 (59.2)*	287 (54.8)	45 (45.5)	316 (52.8)	16 (66.7)
Delirium incidence, n (%)	29 (16.6)	103 (22.9)	109 (20.7)	23 (23.2)	125 (20.8)	7 (29.2)
ICU admission, n (%)	20 (11.3)	128 (28.6)*	128 (24.3)	20 (20.2)	134 (22.3)	14 (58.3)*
Complications						
Restraint use, n (%)	17 (9.4)	109 (24.2)*	105 (19.7)	21 (21.2)	120 (19.8)	6 (25.0)
Falls, n (%)	12 (6.7)	22 (4.9)	31 (5.8)	3 (3.0)	33 (5.4)	1 (4.2)
Respiratory failure, n (%)	7 (3.9)	104 (23.1)*	93 (17.5)	18 (18.2)	104 (17.1)	7 (29.2)
ARDS, n (%)	2 (1.1)	74 (16.4)*	63 (11.8)	13 (13.1)	70 (11.5)	6 (25.0)

*$p<0.05$

†Frailty is defined as clinical frailty scale greater ≥ 5.

IQR = interquartile range; CXR = chest x-ray; CRP = C-reactive protein in mg/L; ICU = intensive care unit.

Supplementary appendix 1

Data collection

Patients meeting inclusion criteria were identified by decision support at each site. A trained chart assessor abstracted data using case report forms hosted on a REDCap database. Each chart assessor was trained by a physician investigator at the hospital site (BL, JW, EW, KP, TI, and AV). The first five charts were extracted in duplicate with the physician investigator, and the physician investigator reviewed additional charts when the chart assessor had questions. Five physician investigators were geriatricians (BL, JW, EW, KP, and TI) and one was a family physician (AV). A protocol is available on Open Science Framework (https://osf.io/k4g7a/).

Patient characteristics were extracted from the chart, including age at diagnosis, date of diagnosis, sex (as documented on chart), baseline functional status, place of residence, clinical frailty scale (CFS) [1], and past medical history. Treatment for COVID-19 was recorded, including dexamethasone, remdesivir, tocilizumab, hydroxychloroquine, and antibiotics. Enrolment in COVID-19 clinical trials was documented. Delirium was assessed using a validated chart review tool [2] and we recorded whether delirium occurred on presentation to hospital (delirium prevalence) or during hospitalization (delirium incidence). If delirium was present, characteristics including predominant motor subtype, documentation of agitation, restraint use, and medication treatment were abstracted. Outcomes were recorded, including in-hospital mortality, intensive care unit (ICU) admission, length of stay, and in-hospital complications. Complications were defined as events associated with COVID-19 infection, such as venous thromboembolism, respiratory failure, and cardiovascular events [3]. We also recorded geriatric complications such as in-hospital falls and physical restraint use.

Data processing

Missing or erroneous data (e.g. dates that were outside of the study range or temperatures that were outside of physiologic range) were reviewed by the site physician investigator. Missing CFS was imputed as 6 (severe frailty) for LTC residents and 5 (moderate frailty) for retirement home residents based on local LTC admission criteria and published frailty estimates [4,5]. Missing frailty or functional data from community dwelling patients were estimated by the physician investigator based on available data. If relevant information was not documented in the chart, we did not impute missing frailty data from community dwelling patients because of the diverse range of frailty levels [6].

References

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[6] Kelly S, O'Brien I, Smuts K, O'Sullivan M, Warters A. Prevalence of frailty among community dwelling older adults in receipt of low level home support: a cross-sectional analysis of the North Dublin Cohort. BMC Geriatr 2017;17:121. doi:10.1186/s12877-017-0508-2.

Supplementary table 1: Analysis of dexamethasone's association with various outcomes in the wave 2 vs. entire cohort (including wave 1). The findings were similar.

	Wave 2 only			Waves 1 and 2		
	No Dexamethasone	Dexamethasone	P value	No Dexamethasone	Dexamethasone	P value
	180 (28.5)	451 (71.5)		467 (50.4)	460 (49.6)	
In-hospital death, n (%)	13 (7.4)	168 (37.3)	<0.001	90 (19.4)	172 (37.4)	<0.001
Length of stay, median (IQR)	7.0 (3.0–14.0)	11.0 (7.0–21.0)	<0.001	10.0 (4.0–22.0)	11.0 (7.0–21.0)	0.006
Delirium prevalence, n (%)	66 (37.9)	266 (59.2)	<0.001	225 (48.8)	272 (59.4)	0.002
Delirium incidence, n (%)	29 (16.6)	103 (22.9)	0.103	96 (20.8)	105 (22.9)	0.49
ICU admission, n (%)	20 (11.3)	128 (28.6)	<0.001	80 (17.3)	135 (29.5)	<0.001

IQR = interquartile range; ICU = intensive care unit.

Supplementary table 2: Multivariable model of dexamethasone as main predictor of delirium incidence in older adults admitted to acute care hospitals with COVID-19 in wave 2.

Variables	Unadjusted OR	Adjusted OR	P value
Dexamethasone use	1.49 (0.96–2.39)	1.18 (0.73–1.95)	0.502
Age (each 5 year increase)	1.13 (1.02–1.26)	1.14 (1.01–1.29)	0.044
Dementia	1.63 (1.05–2.48)	1.40 (0.84–2.33)	0.201
Clinical frailty scale	1.16 (1.02–1.32)	1.12 (0.95–1.34)	0.179
ICU	2.26 (1.48–3.44)	3.11 (1.93–5.02)	<0.001
Hosmer-Lemeshow test: p=0.108 C-statistic: 0.675			

OR = odds ratio; ICU = intensive care unit admission

Supplementary table 3: A comparison of waves 1 and 2 of COVID-19 patients admitted to rehabilitation or long-term care hospitals.

	Cohort	Wave 1	Wave 2	p-value
n (%)	115 (100)	19 (16.5)	96 (82.5)	
Age, median (IQR)	86.0 (78.5–91.0)	90.0 (85.5–92.0)	85.5 (78.0–90.3)	0.094
Female, n (%)	72 (62.6)	11 (57.9)	61 (63.5)	0.837
Rehabilitation hospital, n (%)	44 (38.3)	1 (5.3)	43 (44.8)	0.001
Long-term care, n (%)	71 (61.7)	18 (94.7)	53 (55.2)	0.001
Clinical frailty scale, mean (SD)	6.80 (1.17)	6.89 (1.33)	6.78 (1.14)	0.701
Frail (CFS ≥5), n (%)	109 (94.8)	18 (94.7)	91 (94.8)	1
Comorbidities, n (%)				
Dementia	56 (48.7)	11 (57.9)	45 (46.9)	0.531
Falls	53 (46.9)	10 (52.6)	43 (45.7)	0.767
Heart failure	17 (14.9)	1 (5.3)	16 (16.8)	0.347
Coronary artery disease	27 (23.7)	3 (15.8)	24 (25.3)	0.554
Chronic kidney disease	13 (11.4)	1 (5.3)	12 (12.6)	0.598
Stroke	21 (18.4)	5 (26.3)	16 (16.8)	0.517
Hypertension	68 (59.6)	14 (73.7)	54 (56.8)	0.267
Diabetes	38 (33.3)	5 (26.3)	33 (34.7)	0.657
Chronic obstructive pulmonary disease	9 (7.9)	2 (10.5)	7 (7.4)	1
Cancer	25 (22.1)	7 (38.9)	18 (18.9)	0.119
Presenting characteristics				
Any infiltrate on chest x-ray, n (%)	7 (7.3)	0 (0.0)	7 (7.8)	1
Maximum temperature (ºC) on presentation, median (IQR)	37.5 (36.9–38.0)	37.7 (37.2–38.0)	37.5 (36.9–38.0)	0.72
Outcomes, n (%)				
Death	28 (24.3)	7 (36.8)	21 (21.9)	0.273
Delirium	17 (14.8)	3 (15.8)	14 (14.6)	1
Any complications	44 (38.3)	4 (21.1)	40 (41.7)	0.152
Complications				
Fall	19 (16.5)	2 (10.5)	17 (17.7)	0.666
Pneumonia	16 (13.9)	0 (0.0)	16 (16.7)	0.12
Aspiration	2 (1.7)	2 (10.5)	0 (0.0)	0.025
Respiratory failure	8 (7.0)	1 (5.3)	7 (7.3)	1
ARDS	4 (3.5)	1 (5.3)	3 (3.1)	1
Restraints	0 (0)	0 (0)	0 (0)	1
Treatment				
Dexamethasone	25 (21.7)	0 (0.0)	25 (26.0)	0.027
Azithromycin	7 (6.1)	1 (5.3)	6 (6.2)	1
Other antibiotics	16 (13.9)	1 (5.3)	15 (15.6)	0.407

IQR = interquartile range; SD = standard deviation; CFS = clinical frailty scale; ARDS = acute respiratory distress syndrome.

CARE case report guidelines

CARE Checklist of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Line
Title	**1**	The diagnosis or intervention of primary focus followed by the words "case report"	**title page**
Key Words	**2**	2 to 5 key words that identify diagnoses or interventions in this case report, including "case report"	**title page**
Abstract (no references)	**3a**	Introduction: What is unique about this case and what does it add to the scientific literature?	**Abstract page**
	3b	Main symptoms and/or important clinical findings	**Abstract page**
	3c	The main diagnoses, therapeutic interventions, and outcomes	**Abstract page**
	3d	Conclusion—What is the main "take-away" lesson(s) from this case?	**Abstract page**
Introduction	**4**	One or two paragraphs summarizing why this case is unique (**may include references**)	**Page 1, lines 2-17**
Patient Information	**5a**	De-identified patient specific information.	**Page 1, 17-19**
	5b	Primary concerns and symptoms of the patient.	**Page 2, 32-43**
	5c	Medical, family, and psycho-social history including relevant genetic information	**Page 2, 32-43**
	5d	Relevant past interventions with outcomes	**not applicable**
Clinical Findings	**6**	Describe significant physical examination (PE) and important clinical findings.	**Not applicable**
Timeline	**7**	Historical and current information from this episode of care organized as a timeline	**not applicable**
Diagnostic Assessment	**8a**	Diagnostic testing (such as PE, laboratory testing, imaging, surveys).	**Page 2, 32-43**
	8b	Diagnostic challenges (such as access to testing, financial, or cultural)	**Not applicable**
	8c	Diagnosis (including other diagnoses considered)	**Page 2, 32-43**
	8d	Prognosis (such as staging in oncology) where applicable	**not applicable**
Therapeutic Intervention	**9a**	Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care)	**Page 5, 90-112**
	9b	Administration of therapeutic intervention (such as dosage, strength, duration)	**Page 5, 90-112**
	9c	Changes in therapeutic intervention (with rationale)	**Page 5, 90-112**
Follow-up and Outcomes	**10a**	Clinician and patient-assessed outcomes (if available)	**Page 5, 90-99**
	10b	Important follow-up diagnostic and other test results	**Not applicable**
	10c	Intervention adherence and tolerability (How was this assessed?)	**Page 5, 106-129**
	10d	Adverse and unanticipated events	**Page 5, 95-99**
Discussion	**11a**	A scientific discussion of the strengths AND limitations associated with this case report	**Page 9, 190-201**
	11b	Discussion of the relevant medical literature **with references**.	**Page 7, 142-189**
	11c	The scientific rationale for any conclusions (including assessment of possible causes)	**Page 7, 142-189**
	11d	The primary "take-away" lessons of this case report (without references) in a one paragraph conclusion	**Page 10. 202-206**
Patient Perspective	**12**	The patient should share their perspective in one to two paragraphs on the treatment(s) they received	**Not applicable**
Informed Consent	**13**	Did the patient give informed consent? Please provide if requested	**Yes ☐ No ☒**