Clinical course and mortality in older patients with COVID-19: a cluster-based study in Hong Kong

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ABSTRACT

Introduction: Compared with previous waves of the coronavirus disease 2019 (COVID-19) pandemic in Hong Kong, the third wave involved a greater number of frail older patients. Because local healthcare policy required hospitalisation for all older adults with COVID-19, we aimed to investigate the clinical course and outcomes in such patients.

Methods: This retrospective observational study included all patients aged ≥65 years who were admitted to Tuen Mun Hospital for management of COVID-19 between 1 July 2020 and 31 August 2020. We reviewed baseline characteristics, clinical presentation, laboratory results, complications, and outcomes. We also investigated the associations of age and Clinical Frailty Scale (CFS) score with in-patient mortality.

Results: In total, 101 patients were included (median age, 73 years); 52.5% were men and 85% had at least co-morbid chronic disease. The most common symptoms were fever (80.2%) and cough (63.4%). Fifty-two patients (51.5%) developed hypoxia, generally on day 8 (interquartile range, 5-11) after symptom onset. Of the 16 patients who required intensive care unit support, 13 required mechanical ventilation. The overall mortality rate was 16.8%. Patients aged 65-69, 70-79, 80-89, and ≥90 years had mortality rates of 9.1%, 10%, 30%, and 25%, respectively. Patients with CFS scores of 1-2, 3-4, 5-6, and ≥7 had mortality rates of 5.7%, 14.7%, 23.5%, and 40%, respectively. A linear relationship was confirmed between the two mortality trends.

Conclusion: Clinical deterioration was common in older patients with COVID-19; their overall mortality rate was 16.8%. Mortality increased linearly with both age and CFS score.

Hong Kong Med J 2022;28:215–22
https://doi.org/10.12809/hkmj219367

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This article was published on 10 Jun 2022 at www.hkmj.org.

New knowledge added by this study

- Clinical deterioration occurred in >50% of older patients (aged ≥65 years) with coronavirus disease 2019 (COVID-19).
- The median time to hypoxia was 8 days after symptom onset.
- Age and frailty each had a linear relationship with in-patient mortality.

Implications for clinical practice or policy

- Frail older patients had less favourable COVID-19 outcomes.
- Frailty screening should be performed universally in older adults with COVID-19 to enable early risk stratification, regardless of presenting symptoms.

Introduction

Hong Kong faced a third wave of the coronavirus disease 2019 (COVID-19) pandemic, from July to September 2020. Whereas the first two waves mainly consisted of imported cases and generally affected younger patients, the third wave mainly consisted of local cases and their respective epidemiological associations. There were multiple outbreaks in residential care homes for older adults. The overall mortality rate increased from 0.69% in late June 2020 to 2% in late October 2020.[1]

Multiple studies have shown that advanced age and co-morbidities are risk factors for mortality in patients with COVID-19.[2-4] Observational studies focused on older patients have reported in-hospital mortality rates of 19.2% to 35.9%.[5,6] However, findings in other countries might not be generalisable to Hong Kong because of considerable variations in disease surveillance, hospitalisation thresholds, and treatment guidelines worldwide. Therefore, an in-depth study of older adults with COVID-19 in Hong Kong is needed.

In 2020, Hong Kong had one of the highest rates of COVID-19–related hospitalisation worldwide.

老年新冠病毒患者的臨床病程及死亡率：香港新界西聯網研究

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目的：與過往兩波疫情相比，香港第三波新冠病毒疫情涉及更多老年患者。基於現行政策，所有65歲或以上的新冠患者皆須接受留院隔離。本研究旨在探討這組患者的臨床病程及死亡率。

方法：這項回顧性研究收集於2020年7月1日至8月31日期間入住屯門醫院的65歲或以上新冠病毒患者資料，檢視患者的基礎特性、臨床病徵、化驗結果、併發症及臨床結果。本研究亦分析患者年齡及臨床衰弱評估量表（CFS）分數與死亡率之間的關聯。

結果：共101名患者被納入研究，年齡中位數為73歲，當中52.5%男性，85%至少有一種長期病患。常見病徵有發燒（80.2%）及咳嗽（63.4%）。52名病人（51.5%）出現缺氧，普遍由病發起第8天發生（四分位距5-11天）。共16名病人需要接受深切治療，其中13人需接受入侵性呼吸機支援。整體死亡率為16.8%。65至69歲、70至79歲、80至89歲、以及90歲或以上的患者死亡率分別為9.1%、10%、30%以及25%。CFS分數為1-2、3-4、5-6以及7-9的患者死亡率分別為5.7%、14.7%、23.5%以及40%。年齡及衰弱程度皆與死亡率之間存在線性關係。

結論：病情惡化乃老年新冠患者間的常見現象，其整體死亡率為16.8%。死亡率亦會隨年齡及CFS分數而出現線性上升。

The local healthcare policy required hospitalisation of all patients aged ≥65 years who had COVID-19; those patients were then admitted to isolation wards, regardless of disease severity. This unique situation enabled us to perform a comprehensive review of the clinical course and outcomes of older patients with COVID-19 in Hong Kong. We compared mortality rates among age-groups and frailty levels to determine whether such factors had predictive value for survival.

Methods

Study design and data collection

This retrospective observational study included patients aged ≥65 years who were admitted to Tuen Mun Hospital, Hong Kong, for management of polymerase chain reaction–confirmed COVID-19 between 1 July 2020 and 31 August 2020. Cases were identified from the hospital's Infectious Disease Team database. We excluded patients who had previously been discharged for COVID-19 and readmitted for other causes, as well as patients who had not been discharged by 31 October 2020 (ie, the date of study commencement).

Hospitalised cases were managed in accordance with standardised practices; routine nursing and medical care were provided under the supervision of infectious disease specialists. Each patient's clinical data (ie, baseline characteristics, co-morbidities, clinical presentation, laboratory findings, treatment, clinical outcomes, and complications) were retrieved from electronic medical records. The 2007 version of the Clinical Frailty Scale (CFS) was used to assess frailty with scores from 1 (very fit) to 9 (terminally ill).[7] The CFS scores were retrospectively derived on the basis of patient co-morbidities, premorbid mobility, and levels of function; these factors were determined using clinical notes, medical and nursing admission assessments, and allied health records. Presenting symptoms and onset dates were reported by patients or their caregivers. Chronic heart disease was defined as any ischaemic or valvular heart disease, arrhythmia, and/or heart failure. Chronic respiratory disease was defined as asthma, chronic obstructive pulmonary disease, bronchiectasis, and/or obstructive sleep apnoea. Chronic kidney disease was defined as chronic kidney disease stage ≥3a. Viral load was determined by the cycle threshold (CT) value in polymerase chain reaction analysis of specimens from the respiratory tract; this value reflected the number of amplification cycles required to produce a detectable amount of viral RNA and was inversely proportional to the viral load. Laboratory results were recorded at baseline unless otherwise specified.

Outcomes

Primary outcomes were the clinical course and outcomes of patients, including their clinical presentation, laboratory findings, treatment, clinical deterioration (defined as hypoxia onset, mechanical ventilation requirement, or intensive care unit [ICU] admission), complications (eg, acute kidney injury, liver impairment, superinfection, thromboembolic, and acute ischaemic events), and in-patient mortality. We compared these findings between survivors and non-survivors. Secondary outcomes were the mortality rates according to age-group and frailty level.

Hypoxia was defined as oxygen desaturation that resulted in a need for supplemental oxygen. In accordance with the KDIGO (Kidney Disease: Improving Global Outcomes) 2012 acute kidney injury guideline,[8] acute kidney injury was defined as an increase in serum creatinine by >26.5 mmol/L within 48 hours or an increase to ≥1.5-fold above baseline, where baseline presumably occurred within the previous 7 days. Liver impairment was defined as an increase of >3-fold above the upper normal limit of serum alanine aminotransferase. Superinfection was defined as secondary bacterial, viral, or fungal infection that occurred ≥48 hours after admission.

Statistical analysis

Statistical analyses were performed using SPSS (Window version 22.0; IBM Corp, Armonk [NY], Unite States). All continuous variables in this study had skewed distributions using the Kolmogorov–

Smirnov test and were expressed as medians with interquartile ranges (IQRs), while categorical variables were expressed as numbers with percentages (%). The Mann-Whitney *U* test was used to compare non-parametric continuous data between groups. As appropriate, the Chi squared test or Fisher's exact test was used to compare categorical variables. The Cochran–Armitage trend test was used to assess mortality trends. All statistical tests were two-sided and P<0.05 was considered indicative of statistical significance.

Results

Study population and baseline characteristics

During the study period, 427 patients were admitted to Tuen Mun Hospital for management of COVID-19. After the exclusion of paediatric patients and adults aged <65 years (n=323), as well as older adults who had not yet been discharged by the study date (n=3), 101 patients were included in the study.

Baseline patient characteristics are shown in Table 1. The median age was 73 years (range, 65-96); 99% of patients were Chinese, 52.5% were men, and 28.7% were old age home residents. Furthermore, 30.7% had at least mild frailty (CFS score ≥5). Overall, 85% of the older patients had at least one co-morbid chronic disease, including hypertension (73.3%); diabetes mellitus (37.6%); hyperlipidaemia (50.5%); chronic heart (14.9%), lung (6.9%), or kidney (5.9%) diseases; stroke (15.8%); dementia (9.9%); obesity (3%); and active malignancy (3%).

Presentation and laboratory findings

Patients were generally admitted 3 days (IQR, 1-6) after symptom onset (Table 1). Only 4% of patients

TABLE 1. Baseline characteristics and clinical presentation*

	All patients (n=101)	Survived (n=84)	Died (n=17)	P value
Baseline characteristics				
Age, y	73 (68-83)	72 (68-82.75)	82 (73-85.5)	0.028
Male sex	53 (52.5%)	44 (52.4%)	9 (52.9%)	0.966
Clinical Frailty Scale score	3 (2-5)	3 (2-5)	5 (3-7)	0.009
Clinical Frailty Scale score ≥5	31 (30.7%)	22 (26.2%)	9 (52.9%)	0.019
Resident of care home	29 (28.7%)	21 (25.0%)	8 (47.1%)	0.067
Active smoker	3 (3.0%)	3 (3.6%)	0	1.000
Active drinker	3 (3.0%)	3 (3.6%)	0	1.000
Hypertension	74 (73.3%)	60 (71.4%)	14 (82.4%)	0.353
Diabetes mellitus	38 (37.6%)	31 (36.9%)	7 (41.2%)	0.740
Hyperlipidaemia	51 (50.5%)	40 (47.6%)	11 (64.7%)	0.199
Obesity	3 (3.0%)	3 (3.6%)	0	1.000
Chronic heart disease	15 (14.9%)	15 (17.9%)	0	0.068
Chronic lung disease	7 (6.9%)	4 (4.8%)	3 (17.6%)	0.091
Chronic kidney disease	6 (5.9%)	5 (6.0%)	1 (5.9%)	1.000
Stroke	16 (15.8%)	11 (13.1%)	5 (29.4%)	0.138
Dementia	10 (9.9%)	7 (8.3%)	3 (17.6%)	0.366
Active malignancy	3 (3.0%)	2 (2.4%)	1 (5.9%)	0.428
Clinical presentation				
Time from symptom onset to admission, d	3 (1-6)	3 (2-7)	1.5 (1-3)	0.068
Completely asymptomatic	2 (2.0%)	2 (2.4%)	0	1.000
Fever	81 (80.2%)	66 (78.6%)	15 (88.2%)	0.362
Cough	64 (63.4%)	54 (64.3%)	10 (58.8%)	0.670
Sputum	38 (37.6%)	30 (35.7%)	8 (47.1%)	0.379
Dyspnoea	18 (17.8%)	13 (15.5%)	5 (29.4%)	0.178
Required oxygen on admission	12 (11.9%)	8 (9.5%)	4 (23.5%)	0.115
Diarrhoea	12 (11.9%)	10 (11.9%)	2 (11.8%)	1.000
Anosmia	5 (5.0%)	5 (6.0%)	0	0.583

* Data are shown as median (interquartile range) or No. (%), unless otherwise specified

were asymptomatic on admission, while only 2% of patients remained completely asymptomatic throughout the course of disease. Common presenting symptoms included fever (80.2%), cough (63.4%), sputum (37.6%), dyspnoea (17.8%), diarrhoea (11.9%), and anosmia (5%). Overall, 11.9% of patients required oxygen support on admission.

Laboratory findings are shown in Table 2. The median trough CT value was 16.6. Lymphopenia and hyponatraemia were common; the median trough lymphocyte count and sodium level were 0.6 × 10^9/L and 133 mmol/L, respectively. Elevated levels of lactate dehydrogenase, C-reactive protein, D-dimer, and ferritin were also common.

Treatment

Antiviral drugs were administered to 86.1% of patients, while antibiotics were administered to 83.2% of patients. During the study period, combined administration of lopinavir-ritonavir and interferon beta-1b was the most commonly used COVID-19-specific antiviral treatment approach. Other COVID-19 treatments (eg, systemic steroid, remdesivir, tocilizumab, convalescent plasma, and extracorporeal blood purification) were administered in accordance with each patient's clinical indications. Systemic steroid treatment was administered to 48.5% of patients; it was mostly administered to patients who developed hypoxia. Overall, 4% of patients received convalescent plasma, 8% required renal replacement therapy, and 1% required extracorporeal membrane oxygenation.

Clinical outcomes and complications

Clinical deterioration occurred in more than half of the older patients. Fifty-two patients (51.5%) developed hypoxia, generally on day 8 (IQR, 5-11) after symptom onset. The outcomes of the 52 patients who developed hypoxia are shown in Figure 1; among the 16 patients who received ICU support, 13 required mechanical ventilation and six died. Three patients did not require mechanical ventilation after

TABLE 2. Laboratory results*

	All patients (n=101)	Survived (n=84)	Died (n=17)	P value
Trough CT value	16.6 (15.4-20.4)	17.2 (15.7-21.4)	15.4 (13.9-17.8)	0.005
Baseline lymphocyte count, × 10^9/L	0.9 (0.7-1.3)	0.9 (0.7-1.3)	0.9 (0.7-1.2)	0.541
Trough lymphocyte count, × 10^9/L	0.6 (0.4-0.9)	0.7 (0.4-1)	0.4 (0.2-0.55)	<0.001
Neutrophil count, × 10^9/L	3.7 (2.7-5.15)	3.6 (2.7-5)	4.4 (2.75-6.35)	0.238
Platelet count, × 10^9/L	192 (154-231)	191 (155.3-231.5)	194 (133.5-235)	0.747
INR	1 (1.0-1.1)	1 (1-1.1)	1.1 (1-1.1)	0.032
APTT, sec	25.8 (24.1-29.1)	25.8 (24-28)	28.5 (24.2-31.9)	0.131
Baseline sodium, mmol/L	137 (135-140)	137 (135-140)	138 (136.5-140.5)	0.353
Trough sodium, mmol/L	133 (130-135.5)	133 (128.25-135)	133 (130.5-138)	0.181
Baseline ALT, U/L	21 (13.3-32)	22 (14-34)	17 (10.5-31)	0.197
Peak ALT, U/L	52 (24-121)	48.5 (23.3-101.5)	62 (28-287.5)	0.309
Albumin, g/L	37 (34-40.5)	38 (34-41.75)	36 (35.5-39)	0.360
Glucose, mmol/L	6.6 (5.6-8.6)	6.4 (5.6-9.08)	6.6 (5.8-7.6)	0.986
Baseline CK, U/L	94 (60-166)	94 (62-169)	101.5 (48.8-162.3)	0.970
Peak CK, U/L	131 (75-253)	117 (71-234)	225.5 (134.8-328.3)	0.014
Baseline LDH, U/L	236 (200-294.5)	231 (198.3-295.3)	244 (214.5-284)	0.448
Peak LDH, U/L	341 (273-451.5)	326 (268.5-419.8)	522 (214.5-912.5)	0.014
Baseline CRP, mg/L	27 (7.7-68.1)	19.1 (4.7-48.4)	57 (9.5-85.4)	0.242
Peak CRP, mg/L	102 (58.5-161)	90.1 (41.8-146)	148 (89.1-244.5)	0.008
D-dimer, ng/mL	956 (585-1480)	897 (544-1295)	2461 (802-2214)	0.209
Procalcitonin, ng/mL	0.25 (0.25-0.25)	0.25 (0.25-0.25)	0.28 (0.25-0.36)	0.004
Ferritin, pmol/L	1973 (1087-4953)	1942.5 (966-4372)	2791 (1339-9487)	0.070
HbA1c, %	6.4 (5.7-7.5)	6.4 (5.8-7.82)	6.2 (5.6-7)	0.343

Abbreviations: ALT = alanine aminotransferase; APTT = activated partial thromboplastin time; CK = creatinine kinase; CRP = C-reactive protein; CT = cycle threshold; HbA1c = haemoglobin A1c; INR = international normalised ratio; LDH = lactate dehydrogenase

* Data are shown as median (interquartile range), unless otherwise specified

ICU admission; all three survived. Thirty-six patients with hypoxia were admitted to general wards because they were not candidates for ICU admission or did not require intensive care; of these 36 patients, 25 survived and 11 died. All 11 patients who died without ICU support had a do-not-resuscitate order and thus did not receive cardiopulmonary resuscitation. Among the 49 patients who did not develop hypoxia, all survived. The overall mortality rate was 16.8% (n=17); the mortality rate among patients who developed hypoxia was 32.7%. Among all ICU patients and among ICU patients who required mechanical ventilation, the mortality rates were 37.5% and 46.2%, respectively.

Acute kidney injury and liver impairment each occurred in 25.7% of patients (Table 3). Superinfection occurred in 17.8% of patients, while delirium occurred in 5.9% of patients. Three patients (3%) experienced thromboembolic or ischaemic events: deep vein thrombosis, acute ischaemic stroke, and acute myocardial infarction (n=1 each). The median time from admission to discharge was 18.5 days (IQR, 12-26), while the median time from admission to death was 15 days (IQR, 10-30).

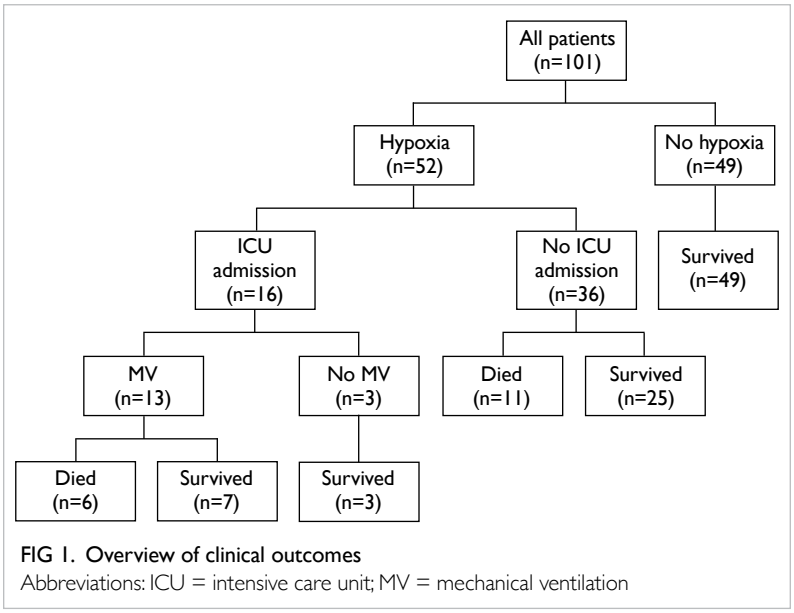

FIG 1. Overview of clinical outcomes
Abbreviations: ICU = intensive care unit; MV = mechanical ventilation

Comparison of survivors and non-survivors

Patients who died during the index admission were older (median age, 72 vs 82 years, P=0.028) and had greater frailty (median CFS score 3 vs 5, P=0.009) [Table 1]. A higher viral load was observed in non-survivors (trough CT value 17.2 vs 15.4, P=0.005). Non-survivors also had a lower trough lymphocyte count (0.7 vs 0.4 × 10^9/L, P<0.001); a higher international normalised ratio (1 vs 1.1, P=0.032); and higher peak levels of creatinine kinase (117 vs 225.5 U/L, P=0.014), lactate dehydrogenase (326 vs 522 U/L, P=0.014), C-reactive protein (90.1 vs 148 mg/L, P=0.008), and procalcitonin (0.25 vs 0.28 ng/mL, P=0.004) [Table 2]. More non-survivors had acute kidney injury (15.5% vs 76.5%, P<0.001) and superinfection (13.1% vs 41.2%, P=0.006) [Table 3].

Impacts of age and frailty on mortality

The mortality rates in patients aged 65-69, 70-79, 80-89, and ≥90 years were 9.1% (3/33), 10% (3/30), 30% (9/30), and 25% (2/8), respectively (Fig 2). Patients who were very fit and well (CFS score 1-2) had a mortality rate of 5.7% (2/35); patients who were managing well or vulnerable (CFS score 3-4) had a mortality rate of 14.7% (5/34); patients with mild to moderate frailty (CFS score 5-6) had a mortality rate of 23.5% (4/17); and patients with at least severe frailty (CFS score ≥7) had a mortality rate of 40%

TABLE 3. Outcomes and complications*

	All patients (n=101)	Survived (n=84)	Died (n=17)	P value
Clinical deterioration				
Time from symptom onset to hypoxia, d	8 (5-11)	9 (6-11)	7 (4.5-11)	0.405
Hypoxia	52 (51.5%)	35 (41.7%)	17 (100%)	<0.001
ICU admission	16 (15.8%)	10 (11.9%)	6 (35.3%)	0.016
Mechanical ventilation	13 (12.9%)	7 (8.3%)	6 (35.3%)	0.002
Complications				
Acute kidney injury	26 (25.7%)	13 (15.5%)	13 (76.5%)	<0.001
Liver impairment	26 (25.7%)	19 (22.6%)	7 (41.2%)	0.110
Delirium	6 (5.9%)	4 (4.8%)	2 (11.8%)	0.265
Superinfection	18 (17.8%)	11 (13.1%)	7 (41.2%)	0.006
Thromboembolic/ischaemic event	3 (3.0%)	1 (1.2%)	2 (11.8%)	0.073

Abbreviation: ICU = intensive care unit
* Data are shown as median (interquartile range) or No. (%), unless otherwise specified

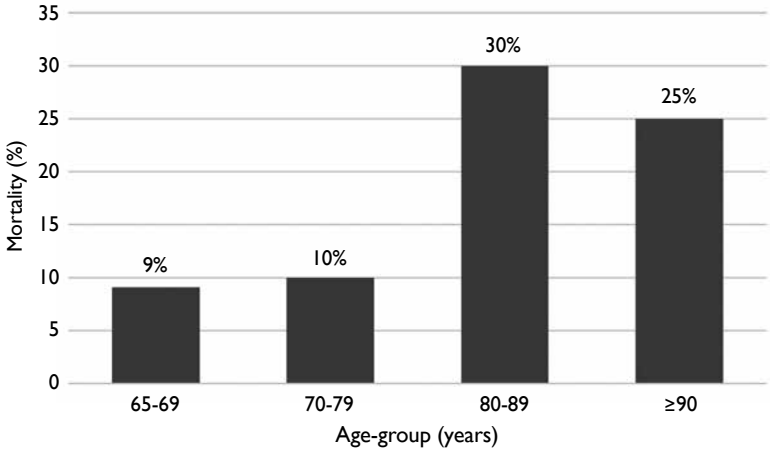

FIG 2. Mortality rate according to age-group

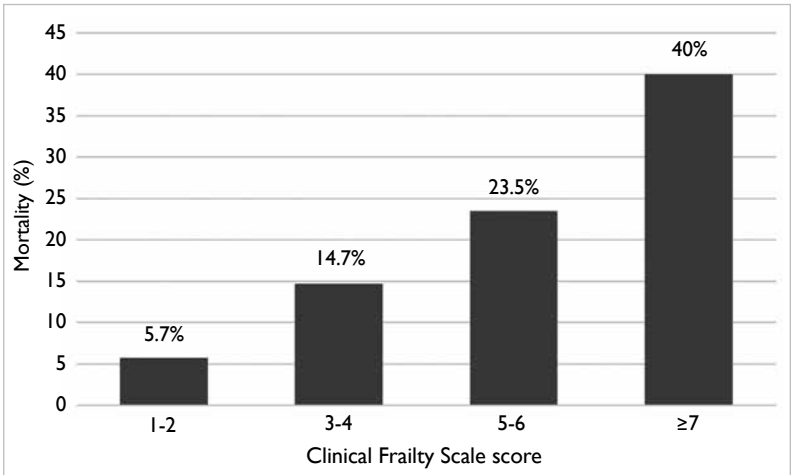

FIG 3. Mortality rate according to Clinical Frailty Scale score

(6/15) [Fig 3]. The Cochran–Armitage trend test showed that mortality linearly increased with both age (P=0.031) and CFS score (P=0.003).

Discussion

As of 31 October 2020, there were >5300 COVID-19 cases in Hong Kong; the median age was 43 and the overall case fatality rate was 2%.[1] Previous studies have shown that mortality is much higher among older patients. A large prospective cohort study of 20 000 hospitalised patients with COVID-19 in the United Kingdom (median age, 74 years) revealed a mortality rate of 26%.[3] Another cohort study of 5700 hospitalised patients with COVID-19 in New York revealed a mortality rate of 32.7% among the 1425 patients aged >60 years.[9] Because hospitalisation is required for older adults (aged ≥65 years) with COVID-19 in Hong Kong, our in-patient mortality of 16.8% can be regarded as a close approximation of the case fatality rate for this age-group; this was significantly higher than the case fatality rate in the general population. The broad hospitalisation requirement for older adults in Hong Kong may also explain the substantially lower mortality rate in this study, compared with studies in countries where only patients with severe disease were hospitalised.

Our findings suggest that older patients tend to have symptomatic COVID-19. Fever occurred in >80% of patients; only 2% of patients remained completely asymptomatic throughout the course of disease. A meta-analysis of 41 studies by He et al,[10] which involved >50 000 patients from all age-groups, revealed that the pooled percentage of asymptomatic COVID-19 was 15.6%—this was much higher than the rate in the present study. In addition to the possible effects of age differences, the high rate of symptoms reported in this study could also be related to the early identification and active screening of high-risk patients (eg, patients who had contact with positive cases and were placed under close medical surveillance in quarantine centres).

We observed some differences between survivors and non-survivors in terms of baseline patient characteristics, laboratory findings, and complications. Non-survivors were significantly older and had greater frailty; they also had a higher viral load, lower lymphocyte count, higher inflammatory marker levels, and higher incidences of acute kidney injury and superinfection. Because of sample size limitations, we did not perform multivariate analyses of each factor potentially associated with mortality; however, we observed some trends. For example, death occurred in 29% of patients with at least mild frailty (CFS score ≥5) and 33.3% of patients who required supplemental oxygen on admission; these features might be early indicators of poor prognosis. Furthermore, death occurred in 50% of patients with acute kidney injury and 38.9% of patients with superinfection. Such complications could also be indicators of poor prognosis because the associated mortality rates were not negligible.

In this study, patients generally showed clinical deterioration on day 8 after symptom onset. This is consistent with the findings by Zhou et al[2] in Wuhan, where the times from illness onset to dyspnoea and sepsis were 7 and 9 days, respectively. Additionally, the overall rate of deterioration was high among older patients, such that 51.5% developed hypoxia during the course of disease. This was comparable to the results of a study by Mostaza et al,[6] in which exacerbation of dyspnoea occurred in 43% of 400 older patients. These high rates are a cause for concern because older patients with COVID-19 are reportedly more susceptible to silent hypoxia,[11,12] which may be missed without close monitoring; thus, subsequent treatment may be delayed.

In this study, a do-not-resuscitate order had been issued for each of the 11 hypoxic patients who died after a lack of ICU support. These patients constituted 10.9% of all older patients in the study; they were substantially older and had greater frailty, both of which were contra-indications for ICU admission. The care team was able to promptly identify these patients and involve them (and/or their families) in advanced care planning. Because resources are limited during the COVID-19 pandemic, it is important to identify patients at risk of deterioration, as well as patients with poor reserve who are unlikely to survive the disease. In the early stages of the global pandemic, some countries proposed age limits for access to intensive care because of crises in their healthcare systems; such proposals created ethical dilemmas and allegations of ageism.[13,14] Frailty screening was proposed to replace the age criterion for resource allocation[13]; accordingly, we compared its association with in-patient mortality to the association of age with in-patient mortality.

Frailty has been defined as an ageing-related decline in physiological reserve, which leads to increased vulnerability to stress. It has been associated with poor clinical outcomes in older adults[7,15,16] and has been used to predict chest infection–related mortality.[17] The CFS is a simple nine-point tool for assessing frailty. Compared with non-frail patients (CFS score 1-4), at least mild frailty (CFS score ≥5) has been independently associated with all-cause mortality in hospitalised patients.[18]

A few studies have shown a relationship between frailty and COVID-19–related mortality. In a European multicentre cohort study of in-patients with COVID-19, Hewitt et al[19] found that the hazard ratio for mortality increased with increasing CFS score; compared with CFS score 1-2, the adjusted hazard ratios were 1.55 for CFS score 3-4, 1.83 for CFS score 5-6, and 2.39 for CFS score 7-9. Disease outcome was more accurately predicted by frailty than by age or co-morbidity. Moreover, mortality rates in patients with CFS scores 5-6 and ≥7 were 30.9% and 41.5%, respectively; these were broadly similar to our findings. In the United Kingdom, Brill et al[20] conducted a study of very old patients with COVID-19; they found a significantly higher CFS score (but not significantly older age) among patients who died than among patients who survived. The results of both above studies are consistent with our findings.

In this study, we observed a substantial increase in mortality, from approximately 10% in patients aged 65-79 years to approximately 30% in patients aged 80-89 years. However, the mortality rate reached a plateau and did not increase with further increases in age. In contrast, mortality progressively increased with increasing frailty, from 5.7% in patients who were fit and well (CFS score 1-2) to 40% in patients with at least severe frailty (CFS score ≥7). Although both age and frailty had linear statistical relationships with mortality, the linearity was more pronounced for frailty. Our findings support the use of frailty screening at admission for all older patients with COVID-19; this early assessment can predict adverse outcomes, regardless of initial symptoms and disease severity. Rather than age alone, frailty and age should be considered together when making decisions about resuscitation and advanced care planning.

A notable strength of this study was that it provided a comprehensive overview of the clinical course and outcomes in all older patients with COVID-19, over a wide range of disease severity, because of the non-selective hospitalisation policy in Hong Kong. Because all admitted older adults were included in the study, there was no selection bias. Furthermore, because patients who had not been discharged by the study date were excluded from the study, data were available for all clinical outcomes among the included patients.

There were some limitations in this study. First, it had a small sample size. Tuen Mun Hospital was the only designated centre in the New Territories West Cluster in Hong Kong that provided acute care during the index admission for patients with COVID-19; it covered a population of >1 million. Although this was a cluster-based study, the sample size was small and certain statistical tests could not be performed because they were underpowered. Future multicentre or multi-cluster studies may yield more comprehensive results. Second, the CFS score was determined in a retrospective manner; it might have been limited by the availability of functional assessment data from electronic records. While assessments of patients under geriatric care are usually comprehensive, evaluations might have been incomplete for patients who were new to the Hospital Authority. To minimise potential errors, the scores were separately determined by two geriatric specialists, then stratified into four categories of CFS score. Although dedicated prospective assessments are preferable, previous studies have shown that retrospectively determined CFS scores have high precision and reliability, compared with prospectively determined scores.[21] Third, some data were missing. For example, effective reporting of disease symptoms and onset might be difficult for dependent older adults; moreover, some blood tests (eg, procalcitonin, ferritin, and D-dimer) were not performed for some patients. Finally, the results of this study might not be generalisable to other countries or centres because the management of patients with COVID-19 largely depends on local practices. Hospitalisation rates, treatment thresholds, and therapeutic regimens may considerably vary around

the world. Thus, our findings should be carefully interpreted and compared with the results of other studies.

Conclusion

Clinical deterioration was common in older patients with COVID-19. Mortality was high with respect to the overall case fatality rate. Linear relationships with mortality were observed for both age and frailty.

Author contributions

Concept or design: EMYY Tam, YK Kwan.
Acquisition of data: EMYY Tam, YK Kwan, YY Ng.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: EMYY Tam.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Declaration

An abstract of this study was submitted to the Hospital Authority Convention 2021.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

This study was approved by the New Territories West Cluster Research Ethics Committee (Ref No: NTWC/REC/20135).

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