International Journal of Gerontology 16 (2022) 207–212
https://doi.org/10.6890/IJGE.202207_16(3).0008

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Characteristics and Outcomes of Hospitalized Geriatric Patients with COVID-19 Infection in Taiwan

Hsin-Pei Chung [a,b], Kuo-Lun Wu [a,b], Chang-Yi Lin [a,b], Yen-Hsiang Tang [b,c], Chao-Hsien Chen [a,b *], Jou-Chun Wu [a,b], Yen-Ting Chen [a,b], Kuan-Chih Kuo [a,b], Wen-Kuei Chang [a,b]

[a] *Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, MacKay Memorial Hospital, Taipei, Taiwan,* [b] *Department of Medicine, MacKay Medical College, New Taipei City, Taiwan,* [c] *Department of Critical Care Medicine, MacKay Memorial Hospital, Taipei, Taiwan*

ARTICLE INFO

Accepted 17 June 2022

Keywords:
aged,
comorbidity,
COVID-19,
geriatric,
mortality

SUMMARY

Background: Geriatric patients with COVID-19 have had poor clinical outcomes globally, especially during the first wave of the pandemic. In Taiwan, the first wave of the COVID-19 pandemic occurred from May to July 2021. This retrospective study aimed to compare the characteristics and outcomes between geriatric and younger patients with COVID-19 infection.
Methods: A total of 257 confirmed COVID-19 cases who were hospitalized from May to June 2021 were included. Their characteristics and outcomes, including in-hospital mortality, use of mechanical ventilation, and hospital stay, were collected for analysis.
Results: There were 98 elderly patients (aged ≥ 65 years, median, 72.5 (interquartile range, 69.0–78.0) years) and 159 younger patients (aged < 65 years, median 55.0 (46.0–60.0) years). The elderly patients had a significantly higher Charlson comorbidity score (4.0 (3.0–5.0) vs. 1.0 (1.0–2.0), $p < 0.001$), and significantly higher D-dimer, procalcitonin, ferritin, and creatinine levels, but lower albumin level than the younger patients. The elderly group also had higher in-hospital mortality (7.1% vs. 1.9%, $p < 0.05$), were more likely to develop severe disease (83.7% vs. 67.9%, $p < 0.01$), and had a longer hospital stay (15.0 (11.0–23.0) vs. 12.0 (9.0–16.5) days, $p < 0.001$). Nevertheless, the elderly patients did not have a higher risk of using high-flow nasal cannulas (17.3% vs. 15.1%, $p = 0.63$) or mechanic ventilation (23.5% vs. 17.0%, $p = 0.20$).
Conclusion: Elderly COVID-19 patients had significant higher risks of severe disease, mortality, and longer duration of hospitalization, possible due higher rates of comorbidities and pro-inflammatory status.

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1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has infected over 416 million people resulting in 5.8 million deaths worldwide as of February 2022.[1] Age is an important factor associated with the severity of COVID-19 and mortality.[2,3] In the United States, people aged more than 65 years have accounted for 74.4% of deaths during the pandemic.[4] In Taiwan, the proportion of people aged 65 or above reached 14% in 2018, and it is estimated to reach 20% by 2026, when Taiwan will become a super-aged society.[5] Until the end of 2021, 14,603 confirmed cases of COVID-19 and 838 deaths have been reported in Taiwan.[6] Although people aged more than 60 years account for only 33.8% of those infected with COVID-19, they account for 88.8% of the deaths. Most of these cases were reported during the first wave of the pandemic from late May 2021 to the middle of July 2021.[7]

Before COVID-19 vaccine was developed and widely vaccinated, treatment of COVID-19 was difficult. Although several treatments including systemic corticosteroids,[8] remdesivir,[9] tocilizumab,[10] and enoxaparin[11] have been introduced before 2021, supportive care remains the backbone of treatment. Underlying diseases, including cardiovascular disease (CVD), chronic lung disease, hypertension, and diabetes have been associated with developing critical disease or death.[12] In addition, higher white blood cell count, C-reactive protein, procalcitonin, ferritin, D-dimer, lactate dehydrogenase, and creatinine, and lower lymphocyte count and albumin have been significantly associated with COVID-19-related mortality.[13] In addition, an older age itself has been independently associated with COVID-19-related mortality without other risk factors.[14] The mortality rate among geriatric patients in Taiwan was more than 13 folds compared to those aged from 20 to 60 years during 2020–2021 (15.1% vs. 1.1%),[6] which was more prominent compared with other countries.[3] However, to the best of our knowledge, no previous study has focused on geriatric COVID-19-infected patients in Taiwan. Therefore, the aim of this study was to investigate differences in the clinical characteristics of hospitalized geriatric patients compared with younger COVID-19 patients and their hospital outcomes at a tertiary care center in Taiwan.

2. Materials and methods

2.1. Study design and patient selection

This retrospective observational study was conducted at Mac-

* Corresponding author. MacKay Memorial Hospital, Tamsui Branch, No. 45, Minsheng Rd., Tamshui District, New Taipei City 25160, Taiwan.
E-mail address: stardust.macaque@gmail.com (C.-H. Chen)

Kay Memorial Hospital (a tertiary hospital in Taipei, Taiwan), and approved by the Institutional Review Board of MacKay Memorial Hospital (approval number 21MMHIS330e). Adult patients with laboratory-confirmed COVID-19 infection admitted to MacKay Memorial Hospital from May to June 2021 were recruited. COVID-19 infection was defined by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) assay result of a specimen collected on a nasopharyngeal swab.

Patients who were under 20 years of age, with repeated hospitalizations, who were transferred to other hospitals, refused to undergo a blood test, or had missing data were excluded. Patients with "do not intubate" (DNI) on electronic medical records were also excluded as they received hospice care.

Electronic medical records, laboratory results and hospital outcomes were retrieved for analysis. Laboratory tests were collected within the first day of hospital admission. The Charlson comorbidity index (CCI) was also calculated according to past medical history.[15] Patients aged between 20 to 65 years old were defined as the younger group, and those aged 65 years or older were defined as the elderly group. Severe COVID-19 infection was defined according to the WHO classification as patients with peripheral oxygen saturation (SpO_2) less than 94% at room air, and patients needing supplemental oxygen to maintain $SpO_2 \geq 94\%$.[16]

2.2. Outcome measurement

The primary outcome was in-hospital mortality, and the secondary outcomes included the use of oxygen, high-flow nasal cannula (HFNC), and mechanical ventilation (MV). The time to mortality and time to first HFNC or MV after admission were also evaluated. The patients were followed until an event, death, or discharge, whichever occurred first.

Propensity score matching was also performed to balance the difference in baseline characteristics and treatment received between two groups. The propensity scores for each patient were generated using a multivariate logistic regression model including variables including hypertension, chronic renal disease (CKD), chronic obstructive pulmonary disease (COPD), CVD, cancer, body mass index, D-dimer, procalcitonin, albumin, ferritin, creatinine, systemic corticosteroid, and remdesivir. Nearest neighbor method was using to match patients under ratio of 1:1 with a tolerant width of 0.1.

2.3. Statistical analysis

Categorical variables were presented as number (± percentage). The frequencies of categorical variables were compared using the chi-squared test or Fisher's exact test. The normality of distribution of continuous variables was tested using the Shapiro-Wilk test. Continuous variables with normal distribution were reported as mean ± standard deviation (SD), and non-normally distributed variables were reported as median (interquartile range [IQR]). Means of two continuous normally distributed variables were compared using the independent samples t-test. The Mann-Whitney U test was used to compare two groups of non-normally distributed variables. For the time-to-event analysis, the log-rank test was used to compare differences in the probability. For all tests, a two-sided p value less than 0.05 was considered to be significant.

We also conducted a multivariant regression to identify the factors related to the mortality among elderly COVID-19 infected patients. Variables with $p < 0.05$ in the univariate logistic regression analysis were considered significant and were included in the multivariable logistic regression model. All data were analyzed using MedCalc version 20.014 for Windows (MedCalc Software Ltd., Ostend, Belgium). Propensity score matching was performed using SPSS Statistics version 28.0.1.1 for Windows (IBM, New York, U.S.)

3. Results

During the study period, a total of 330 patients were admitted with the diagnosis of COVID-19 infection. Patients who could not be confirmed by RT-PCR, those with repeated hospitalizations, those who were transferred to other hospitals, refused to undergo a blood test, or refused intubation during respiratory failure with DNI orders were excluded, and the remaining 257 patients were analyzed (Figure 1). Among them, 159 patients were in the younger group (median age 55.0 (46.0–60.0) years) and 98 patients were in the elderly group (median age 72.5 (69.0–78.0) years).

There were more male (54.9%) than female patients, however there was no significant difference in gender distribution between the younger and elderly groups (Table 1). The patients in the elderly group had a higher CCI (4.0 (3.0–5.0) vs. 1.0 (1.0–2.0), $p < 0.001$), and higher rate of comorbidities (69.4% vs. 45.3%, $p < 0.001$), especially hypertension (60.2% vs. 23.9%, $p < 0.001$), CKD (9.2% vs. 1.9%, $p = 0.01$), COPD (7.1% vs. 1.9%, $p < 0.05$), CVD (10.2% vs. 3.8%, $p = 0.04$) and cancer (10.2% vs. 2.5%, $p = 0.01$) (Table 1). The elderly group also had higher levels of D-dimer (1070 (646.3–1872.0) vs. 598.5 (363.5–1046.0) ng/mL, $p < 0.001$), procalcitonin (0.05 (0.05–0.18) vs. 0.05 (0.05–0.11) ng/mL, $p = 0.01$), ferritin (540.1 (336.6–1011.7) vs. 379.5 (165.1–865.2) ng/mL, $p < 0.001$), and creatinine (1.00 (0.80–1.40) vs. 0.80 (0.70–1.00) mg/dl, $p < 0.001$) than the younger group. However, they had a significantly lower albumin level (3.70 (3.40–4.03) vs. 4.10 (3.70–4.30) g/dL, $p < 0.001$) than the younger group. The elderly group were more likely to receive treatment of systemic corticosteroid (85.7% vs. 75.5%, $p < 0.05$) and remdesivir (49.0% vs. 29.6%, $p = 0.0018$).

The elderly group had higher in-hospital mortality (7.1% vs. 1.9%, $p < 0.05$), were more likely to develop severe disease (83.7% vs. 67.9%, $p < 0.01$), and had a longer hospital stay (15.5 (11.0–23.0) vs. 12.0 (9.0–16.5) days, $p < 0.001$). However, the elderly patients did not have a higher risk of using HFNC (17.3% vs. 15.1%, $p = 0.63$) or MV (23.5% vs. 17.0%, $p = 0.20$) than the younger patients. In the time-to-event analysis, there was no significant increase in the risk of using HFNC or MV (hazard ratio [HR]: 1.34, 95% confidence interval [CI]: 0.78–2.30, p = 0.28), however there was a higher risk of

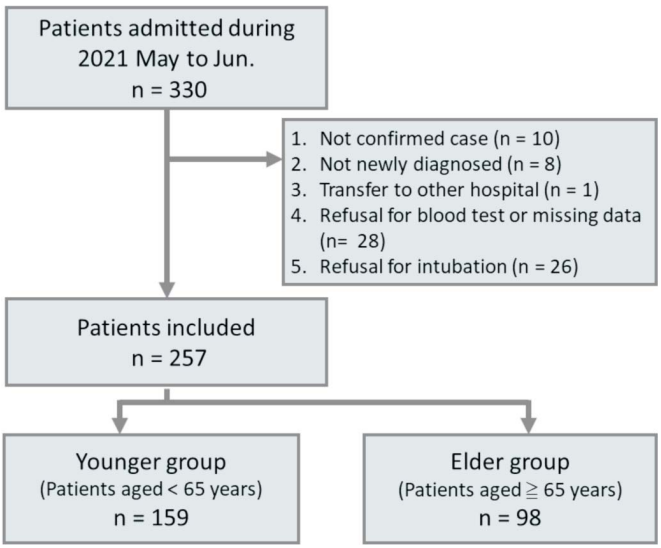

Figure 1. Flowchart of the included patients.

mortality (HR: 4.21, CI: 1.10–16.19, p = 0.04) in the elderly group (Figure 2 and 3).

After propensity score matching, the matching algorithm selected 44 younger patients and 44 elderly patients. The unbalance in comorbidity, laboratory results, and treatment received between two group was no more significant (Table S1). The in-hospital mortality in elderly group was not statistically significant increased after propensity score matching (9.1% vs. 4.5%, $p = 0.68$).

When focusing on severe COVID-19 infection, there were no differences in duration of oxygen therapy (11.0 (6.0–17.0) vs. 10.0

Table 1
Baseline characteristics, laboratory findings and outcomes of the patients with COVID-19 infection.

Characteristics	All patients (n = 257)	Younger group (n = 159)	Elderly group (n = 98)	*p* value
Age, years	61.0 (53.0–71.0)	55.0 (46.0–60.0)	72.5 (69.0–78.0)	< 0.001
Gender				0.75
Male	141 (54.9%)	86 (54.1%)	55 (56.1%)	
Female	116 (45.1%)	73 (45.9%)	43 (43.9%)	
CCI	2.0 (1.0-3.0)	1.0 (1.0-2.0)	4.0 (3.0–5.0)	< 0.001
Comorbidities				
Any of following	140 (54.5%)	72 (45.3%)	68 (69.4%)	< 0.001
Hypertension	97 (37.7%)	38 (23.9%)	59 (60.2%)	< 0.001
Diabetes	72 (28.0%)	41 (25.8%)	31 (31.6%)	0.31
CKD	12 (4.7%)	3 (1.9%)	9 (9.2%)	0.01
COPD	10 (3.9%)	3 (1.9%)	7 (7.1%)	< 0.05
CVD	16 (6.2%)	6 (3.8%)	10 (10.2%)	0.04
Cancer	14 (5.4%)	4 (2.5%)	10 (10.2%)	0.01
BMI, kg/m^2	25.5 (23.2–27.8)	26.0 (23.4–28.5)	24.8 (22.7–26.7)	0.02[a]
Days from symptoms onset or diagnosed to admission	6.0 (2.0–8.0)	6.0 (2.0–8.0)	6.0 (2.0–8.0)	0.94
White blood cell count, $\times 10^9/L$	6.1 (4.48–8.05)	6.0 (4.3–7.7)	6.25 (4.7–8.5)	0.31
Absolute lymphocyte count, $\times 10^9/L$	0.92 (0.58–1.26)	0.98 (0.67–0.28)	0.89 (0.5–0.23)	0.10
D-dimer, ng/mL	760.0 (466.0–1289.3)	598.5 (363.5–1046.0)	1070 (646.3–1872.0)	< 0.001
Procalcitonin, ng/mL	0.05 (0.05–0.13)	0.05 (0.05–0.11)	0.05 (0.05–0.18)	0.01
CRP, mg/dL	4.44 (1.43–10.56)	4.07 (1.22–9.89)	5.36 (2.12–12.04)	0.05
Albumin, g/dL	3.90 (3.60–4.30)	4.10 (3.70–4.30)	3.70 (3.40–4.03)	< 0.001
Ferritin, ng/mL	460.5 (200.8–923.1)	379.5 (165.1–865.2)	540.1 (336.9–1011.7)	< 0.001
LDH, U/L	255.0 (188.8–360.5)	254.5 (175.5–373.5)	255.0 (199.0–359.3)	0.54
Creatinine, mg/dl	0.90 (0.70–1.10)	0.80 (0.70–1.00)	1.00 (0.80–1.40)	< 0.001
Systemic corticosteroid	204 (79.4%)	120 (75.5%)	84 (85.7%)	< 0.05
Remdesivir	95 (37.0%)	47 (29.6%)	48 (49.0%)	< 0.01
Tocilizumab	74 (28.8%)	42 (26.4%)	32 (32.7%)	0.28
Use of oxygen supplement	190 (73.9%)	109 (68.6%)	81 (82.7%)	0.0126
High-flow nasal cannula	41 (16.0%)	24 (15.1%)	17 (17.3%)	0.63
Mechanical ventilation	50 (19.5%)	27 (17.0%)	23 (23.5%)	0.20
Hospital duration of the survivors, days	13.0 (10.0–18.8)	12.0 (9.0–16.5)	15.0 (11.0–23.0)	< 0.001
In-hospital mortality	10 (3.9%)	3 (1.9%)	7 (7.1%)	< 0.05
Discharged alive	247 (96.1%)	156 (98.1%)	91 (92.9%)	

[a] Data of 120 vs. 85 patients were available for BMI.
BMI: body mass index; CCI: Charlson comorbidity index; CKD: chronic kidney disease; COPD; chronic obstructive pulmonary disease; CRP: C-reactive protein; CVD: cardiovascular disease; LDH: lactic dehydrogenase.

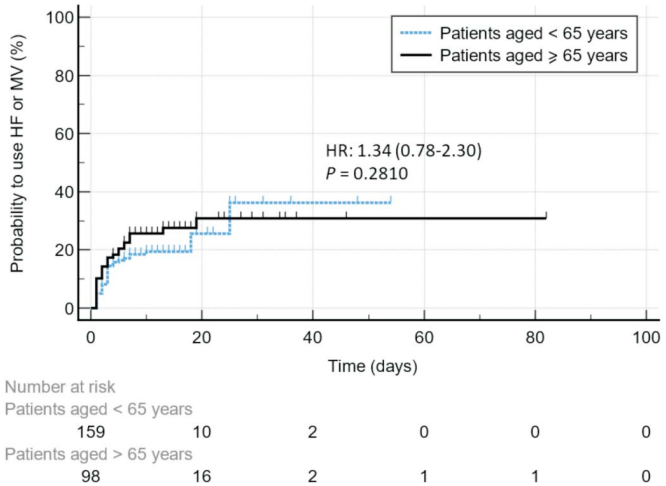

Figure 2. Cumulative probability of invasive or non-invasive ventilator requirement after admission between the elderly and younger patients with COVID-19 infection. HF: high-flow nasal cannula; MV: mechanical ventilation.

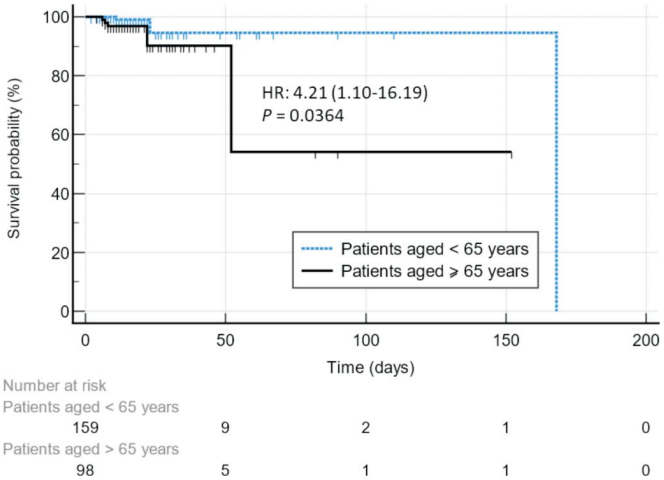

Figure 3. Kaplan-Meier estimates of the cumulative probability of survival after admission between the elderlyand younger patients with COVID-19 infection. HR: hazard ratio.

(5.0–13.0) days, $p = 0.25$), risk of using HFNC or MV (32.9% vs. 29.6%, p = 0.63), and in-hospital mortality (8.5% vs. 2.8%, $p = 0.10$) between the elderly and younger groups (Table 2). However, the hospital stay was longer in the elderly group (15.0 (11.0–22.0) vs. 12.0 (9.5–13.5) days, $p < 0.01$).

Among elderly COVID-19 infected patients, who had diabetes (odd ratio [OR]: 1.8326, 95% CI: 1.1398–34.2723, p = 0.0348), COPD (OR: 6.8800, 95% CI: 1.0589–44.7017, p = 0.0434), elevated procalcitonin (OR: 8.9138, 95% CI: 1.8589–42.7423, p = 0.0062) and CRP (OR: 1.1191, 95% CI: 1.0105–1.2392, p = 0.0307) were related to in-hospital mortality. After multivariant logistic regression, only elderly patients with COPD were statistically significant related to the mortality (Table 3).

4. Discussion

In our retrospective analysis, we found that the elderly patients had a 3.5-fold higher in-hospital mortality rate, higher risk of developing severe COVID-19 infection, and longer hospital stay. The difference of mortality between elderly and younger hospitalized patients were less prominent in our analysis compared to the national statistical data of 13.7-fold in Taiwan.[6]

Aging can cause numerous changes in the immune system, which could increase susceptibility to COVID-19 infection and worsen the clinical prognosis.[17,18] Immunosenescence and inflammaging are considered to be two features of an aging immune system. Defective innate and adaptive immune responses due to senescent immune cells, and aberrant chronic inflammation caused by the production of inflammatory mediators due to weakening of down-regulated innate immune responses driven by regulatory cells may impair the immune response in geriatric patients.[19] In the present study, the elderly group had a trend of lower lymphocyte count but significantly higher inflammatory biomarkers, including ferritin, procalcitonin and D-dimer than the younger group. All of these features have been reported to be predictive factors of mortality in previous studies.[20–23] Dysregulation of the immune system may therefore have played an important role in the dismal prognosis of our elderly group.

Another possible explanation for the higher mortality rate in our elderly group is the higher rate of underlying comorbidities. The elderly group had a significantly higher CCI score than the younger group, with higher rates of hypertension, CVD, chronic obstructive pulmonary disease, chronic kidney disease, and cancer. The CCI has been significantly associated with mortality and disease severity in COVID-19 infection.[24,25] A population-based cohort study of 167,500 patients in Canada found that comorbidities such as hypertension, CVD, chronic obstructive pulmonary disease, chronic kidney disease, and cancer, were predictors of mortality in COVID-19 patients.[26] Several other studies have also emphasized the importance of pre-existing comorbidities on mortality in elderly COVID-19 patients.[27–29]

Table 2
Outcomes during hospitalization between the elderly and younger patients with severe COVID-19 infection.

	Younger group (n = 108)	Elderly group (n = 82)	*p* value
Duration of oxygen therapy, days	10.0 (5.0–13.0)	11.0 (6.0–17.0)	0.25
HFNC or invasive MV	32 (29.6%)	27 (32.9%)	0.63
Duration of HFNC or invasive MV, days	9.0 (6.0–16.5)	9.0 (6.0–18.5)	0.77
Hospital duration of the survivors, days	12.0 (9.5–13.5)	15.0 (11.0–22.0)	< 0.001
In-hospital mortality	3 (2.8%)	7 (8.5%)	0.10
Discharged alive	105 (97.2%)	75 (91.5%)	
Discharged with tracheostomy	2 (1.9%)	1 (1.2%)	> 0.99

HFNC: high-flow nasal canula; MV: mechanical ventilation.

Table 3
Univariate and multivariate logistic regression of the factors related to in-hospital mortality among elderly COVID-19 patients.

	Univariant logistic regression			Multiivariant logistic regression		
	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Age, years	1.0219	0.9124–1.1446	0.7076			
Gender, male	5.1429	0.5950–44.4514	0.1367			
Charlson comorbidity index	1.0826	0.8175–1.4336	0.5796			
Hypertension	1.7130	0.3153–9.3053	0.5331			
Diabetes	1.8326	1.1398–34.2723	0.0348	2.4080	0.3170–18.2940	0.3956
Chronic kidney disease	NA					
Chronic obstructive pulmonary disease	6.8800	1.0589–44.7017	0.0434	12.5695	1.3609–116.0956	0.0256
Cardiovascular disease	1.5185	0.1639–14.0672	0.7130			
Cancer	NA					
Body mass index, kg/m^2	1.0119	0.8167–1.2538	0.9138			
White blood cell count, $\times 10^9/L$	1.0000	0.9999–1.0001	0.8693			
Absolute lymphocyte count, $\times 10^9/L$	0.9995	0.9980–1.0010	0.4747			
D-dimer, ng/mL	1.0002	0.9999–1.0005	0.1130			
Procalcitonin, ng/mL	8.9138	1.8589–42.7423	0.0062	7.389	0.9471–57.6489	0.0564
C-reactive protein, mg/dL	1.1191	1.0105–1.2392	0.0307	1.0448	0.9100–1.1996	0.5338
Albumin, g/dL	0.4731	0.1050–2.1309	0.3297			
Ferritin, ng/mL	1.0001	0.9998–1.0004	0.5790			
Lactic dehydrogenase, U/L	1.0027	0.9999–1.0056	0.0565			
Creatinine, mg/dl	1.2193	0.8498–1.7496	0.2817			
Systemic corticosteroid	NA					
Remdesivir	1.4242	0.3016–6.7265	0.6552			
Tocilizumab	NA					

CI: confidence interval.

In our geriatric patients, the higher rate of comorbidities may also have contributed to their higher possibility of severe disease. The increased mortality in the elderly group was no more significant after balanced comorbidities and pro-inflammation status using propensity score matching, which also indicated higher rate of comorbidities and changing in immune system accompanied aging explained the increased mortality in geriatric patients.

Our results highlight the effect of age on mortality in COVID-19 infection, which is consistent with other studies worldwide.[30–35] A meta-analysis of 611,583 COVID-19 patients by Bonanad et al.[3] reported that mortality increased exponentially in those aged > 60 years, and that the mortality rate was < 1% in those aged < 50 years and highest (29.6%) in those aged > 80 years. In our elderly group, the median age was 72.5 years with an in-hospital mortality rate of 7.1%, which is much lower compared to previous results, ranging from 7.94% to 20.99%.[3] A possible reason for the difference may be due to the delayed pandemic in Taiwan.[36,37] Most studies in Bonanad et al.'s analysis were published before May 2020,[3] however the first wave of the pandemic occurred in Taiwan in May 2021, which is almost 1 year later. Several important protocols such as the use of systemic corticosteroids, remdesivir, tocilizumab, and enoxaparin were established after the first wave of the pandemic in Western countries,[8–11,38] and therefore Taiwan was well prepared. This may have reduced the mortality rate.

In this study, the proportion of critically ill COVID-19 patients was similar among the elderly and younger groups, including the need for HFNC and MV. In addition, when focusing on severe COVID-19 patients, the mortality rate was not significantly different among the elderly and younger groups (8.5% and 2.8%, respectively). Our findings may reinforce previous analysis from Boston in the US that age may not be a significant predictor of intubation.[39] However, in contrast to our results, in the patients who needed MV, older age was associated with an increase in mortality rate per decade of life.[39,40] A possible explanation may be because a disproportionate number of patients with DNI orders were excluded from our study, including 22 patients aged ≥ 65 years of whom 82% died. In contrast, only four patients had DNI orders aged < 65 years, but all eventually died. If we had added these data, the results would have been different.

This study had several limitations. First, it was conducted at a single center in northern Taiwan, and the results may not be generalizable to other areas of Taiwan. Second, the retrospective design of the study resulted in some missing data which may have resulted in bias. In addition, we performed propensity score matched analysis to balance the difference between two group, however, there were only 88 patients left after matching. It may be due to the comorbidities and pro-inflammatory status which were companied with aging, but the decreased number of patients for analysis also resulted in selection bias. Finally, most of the patients included were not followed at our hospital before admission during this pandemic and there were no laboratory results available before their COVID-19 infection. We couldn't conclude that the pro-inflammatory status in the elderly was persistent or only related to the COVID-19 infection. Further well-designed prospective studies are needed to verify our findings.

5. Conclusion

Elderly COVID-19 patients had a significant higher rates of comorbidities and inflammatory status, and this may have increased the risks of severe disease, mortality, and longer duration of hospitalization.

Funding

None.

Conflicts of interest/competing interests

The authors report no conflicts of interest for this work.

Authors' contributions

Study concept and design: HPC, CYL, and CHC. Acquisition of data: HPC, KLW, YHT, CHC, JCW, YTC, KCK, and WKC. Analysis and interpretation of data: All, Drafting of the manuscript: HPC, KLW, CYL and CHC. Drafting and/or critical revision of the manuscript for important intellectual content: HPC, KLW, CYL and CHC. Statistical analysis: CHC. Approval of final manuscript: All.

Supplementary materials

Supplementary materials for this article can be found at http://www.sgecm.org.tw/ijge/journal/view.asp?id=22.

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