Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Clinical characteristics and outcome of COVID-19 pneumonia in elderly subjects

Dear editor,

Since December 2019, some hospitals in Wuhan City, Hubei Province, have successively found multiple cases of unexplained pneumonia which have now been confirmed as a new type of acute respiratory infection caused by a coronavirus infection. The coronavirus isolated from the lower respiratory tract has been named as COVID-19; it has presented an unprecedented challenge for the healthcare community across the world. Based on the rapid increase in the rate of human infection, the World Health Organization (WHO) has classified the COVID-19 outbreak as a pandemic. Respiratory involvement, presenting as mild flu-like illness to potentially lethal acute respiratory distress syndrome or fulminant pneumonia, is the dominant clinical manifestation of COVID-19. Unlike other respiratory diseases, mortality of COVID-19 increased with age while children were observed less susceptible to death. Despite the observation that elderly subjects are more susceptible to severe illness, probably due to underlying co-morbidities such as diabetes, hypertension, cardiovascular and cerebro-vascular diseases,[1,2] literature concerning geriatric patients with COVID-19 pneumonia remained very scant. Most of the studies are editorial commentaries[3] and the clinical studies including patients of varying ages admitted to hospital have only a slight highlight on the association between age and severity of clinical manifestation.[4–6] Further, the majority of data at the moment available often originating from Chinese surveys where elderly patients accounted only for a very limited part of the total. In particular, a paper recently published into your Journal by Wang et al.[2] observed a high fatality rate in the very first days after hospitalization (a median survival of 5 days), and another paper by Liu et al.[6] found a higher mortality rate in elderly than in young and middle-aged patients. However, both these studies considered as elderly patients those aged ≥ 60 years old which is a very different population from that observed in Europe and in particular in Italy, where the elderly (aged ≥ 80 years old) accounted for a large proportion of individuals with severe COVID-19 pneumonia.

In our cohort we included elderly subjects (≥ 80 years old) hospitalized for COVID-19 pneumonia at two North-Italy district hospitals from March 9th to April 30th 2020. We included in this analysis 118 consecutive patients; data on clinical and demographic characteristics, blood test results and COVID-19-related treatments were collected. Survival status and clinical data were compared with a control group of COVID-19 patients aged < 70 years ($n = 109$). Survival analysis was done using a multilevel mixed-effects parametric survival model.

Sixty-eight patients aged ≥ 80 years died (57.6%) after a median time of 4.5 days from admission to emergency department compared to 4 patients (3.7%) in the control group (median time to death in control group: 16.4 days). Table 1 summarizes demographic and clinical characteristics and serum biomarkers of inflammation of the two groups. Older patients were more likely to have lower BMI (24.4 vs 27.3, $p<0.001$), COPD (18.6% vs 3%, $p<0.0001$), earlier access to emergency department from disease presentation (4 vs 6.2 days, $p = 0.02$) and prolonged hospital stay (26 vs 14 days, $p<0.0001$). On the contrary, gastrointestinal symptoms and fever at admission were significantly more frequent in younger subjects. Furthermore, elderly patients had higher white blood cells (11,000/mm^3 vs 6700/mm^3, $p<0.0001$), C-reactive protein (9.8 mg/dL vs 6.5 mg/dL, $p = 0.001$), procalcitonin (0.27 md/dL vs 0.1 mg/dL, $p<0.0001$), LDH (416.5 mg/dL vs 297.6, $p = 0.01$) and D-dimer levels (1100 mg/dL vs 386 mg/dL, $p<0.0001$) at admission. At survival analysis, higher D-dimer levels [HR 1.11 (1.03–1.2), $p = 0.004$] at admission in the emergency department and the combined use of antivirals and hydroxichloroquine [HR 8.42 (2.53–27.98), $p<0.0001$] were independently associated to a higher risk of death.

At our knowledge, this is the first report that evaluated the outcome of COVID-19 pneumonia in subjects ≥ 80 years old. In this subset, we observed a high mortality rate especially in the very first days after hospitalization, probably due to a more rapid disease progression. These findings confirmed those by Wang et al.[2] who observed a median survival of 5 days after admission. Elderly patients have higher levels of inflammatory blood tests at the time of admission in the emergency department; in particular, elevated D-dimer levels was an independent predictor of mortality, confirming the close correlation between this parameter and the severity of COVID-19 disease. Also the use of a treatment including both antivirals and hydroxychloroquine was associated with a higher risk of death. This detrimental effect of the combined treatment could be possibly due to drug-related side effects in the elderly population, but this hypothesis needs to be further confirmed in prospective studies.

In conclusion, our study confirms that the majority of elderly subjects with COVID-19 pneumonia have an unfavorable outcome, especially in the very first days after admission. We also confirm the high importance of D-dimer levels as predictors of mortality and that the treatment with antivirals and hidroxychloroquine is ineffective if not harmful in elderly individuals.

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Table 1
Demographic and clinical characteristics and serum biomarkers of inflammation in subjects ≥ 80 and < 70 years old.

	Age > 80 $n = 118$	Age < 70 $n = 109$	p
Female, *n (%)*	50 (42.4)	35 (32)	0.1
Age, *mean (95% CI)*	86.4 (80–97)	54.8 (46–68)	<0.0001
Body Mass Index, *mean (95% CI)*	24.4 (22.7–26.17)	27.3 (25.4–29.2)	<0.0001
COPD, *n (%)*	22 (18.6)	3 (3)	<0.0001
Any symptom, days from admission, *median (95% CI)*	4 (0–17)	6.2 (0–11)	0.02
Respiratory symptoms, *n (%)*	99 (84)	86 (79)	0.3
Gastrointestinal symptoms, *n (%)*	36 (32)	79 (74)	<0.0001
Fever, *n (%)*	91 (77%)	103 (94)	<0.0001
Length of admission (days), *median (95% CI)*	26 (20–33)	14 (11–17)	<0.0001
Time to death (days), *median (95% CI)*	4.5 (0–30)	16 (12–23)	0.007
Death, *n (%)*	68 (57.6)	4 (3.7)	<0.0001
White Blood Cells/mm^3 *median (95% CI)*	11,000 (5800–16,200)	6700 (5000–8400)	<0.0001
C-Reactive Protein, mg/dL, *median (95% CI)*	9.8 (6.2–13.4)	6.5 (3.3–9.7)	0.001
LDH, mg/dL, *median* (95% CI)	416.5 (325.8–507.2)	297.6 (228–367.2)	0.01
Procalcitonin, mg/dL, *median (95% CI)*	0.27 (0–44.6)	0.1 (0.02–8.2)	<0.0001
D-Dimer, mg/dL, *median (95% CI)*	1100 (150–35,877)	386 (150–40,122)	<0.0001
Fibrinogen, *median (95% CI)*	555.1 (36.6)	534 (36.7)	0.4

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