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Patterns of COVID-19 Hospital Admissions in an Italian Center during the Pandemic Peak: A Large Retrospective Study Highlighting Older Adults

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Abstract

The COVID-19 pandemic has particularly affected older adults who are frail and have multiple chronic conditions. This study retrospectively analyzed the differences in clinical presentation and outcomes among patients admitted to a COVID-19 referral hospital at different stages of the outbreak, emphasizing age, multimorbidity, and functional impairment. Data from 1,264 patients hospitalized between February and June 2020 with radiological and clinical features indicative of COVID-19 pneumonia were reviewed, including demographics, laboratory results, clinical parameters, and outcomes. Patients were categorized based on the admission period (early phase: ascending pandemic wave; later phase: plateau and descending wave), age, initial RT-PCR results for SARS-CoV-2, presence of two or more chronic illnesses, and functional disability. Logistic regression with forward selection identified factors independently linked to in-hospital death. Findings showed that individuals admitted during the later phase were older, more often female, had greater multimorbidity, and were more likely to be functionally dependent. Paradoxically, these patients had less severe respiratory compromise at admission (PaO2/FiO2 268, IQR 174–361 vs. 238, IQR 126–327 mmHg, $p < 0.001$) and lower mortality (22% vs. 27%, $p < 0.001$). Age, compromised respiratory function, positive RT-PCR, higher number of chronic diseases (OR 1.166, 95% CI 1.036–1.313, $p = 0.011$), and functional disability (OR 1.927, 95% CI 1.027–3.618, $p = 0.022$) were associated with increased mortality, whereas admission during the later phase was linked to reduced risk (OR 0.427, 95% CI 0.260–0.700, $p = 0.001$). In conclusion, the timing of hospitalization and the COVID-19 clinical phenotype strongly influenced outcomes, beyond age, multimorbidity, and disability.

Keywords: Prognostic factors, SARS-CoV-2, Frailty, Temporal trends, Comorbidity

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Introduction

During the first wave of the COVID-19 pandemic, the Italian healthcare system faced unprecedented strain, with hospitals overwhelmed by a surge of patients between late February and June 2020 [1, 2]. To accommodate this influx, medical and intensive care units were reorganized to specifically manage patients with suspected or confirmed SARS-CoV-2 infection [3, 4].

Hospitalized individuals frequently experienced severe respiratory compromise, and mortality rates were notably

high. Risk of death is greatest among older adults [5, 6], those with multiple chronic illnesses [6–9], and patients with cardiometabolic conditions [10,11]. Frailty and functional dependency have also been identified as important contributors to poor outcomes in this population [12–14].

Nonetheless, the relationship between these epidemiologic risk factors and clinical outcomes is not always straightforward [15]. COVID-19 exhibits highly heterogeneous presentations, and adverse outcomes may occur independently of age, comorbidities, or frailty [16]. Additionally, some patients with severe respiratory symptoms and imaging indicative of viral interstitial pneumonia repeatedly tested negative for SARS-CoV-2 via nasopharyngeal RT-PCR [17, 18]. While often interpreted as false negatives [19], these cases could reflect a distinct clinical phenotype of COVID-19.

Emerging evidence also indicates that patients admitted during different stages of the pandemic can display variations in disease severity, clinical course, and outcomes [20, 21]. This suggests that the expression of COVID-19 may be influenced not only by patient demographics and comorbidities but also by the phase of the pandemic during which infection occurs.

This single-center retrospective study, conducted at a COVID-19 hub in Northern Italy heavily affected by the first pandemic wave, aimed primarily to compare clinical features and outcomes of patients admitted in two separate pandemic phases. Secondary goals included assessing the prevalence of older age, frailty, and multimorbidity among hospitalized patients with suspected COVID-19 and exploring how these factors relate to in-hospital mortality.

Methods

Study setting and population

This investigation was carried out at the Geriatric-Rehabilitation Department of Parma University Hospital, located in the city of Parma, Emilia-Romagna. The hospital, serving a population of over 300,000 across Parma and neighboring towns, houses around 1,200 beds and is the main facility providing emergency care in the region. During the late February 2020 surge of COVID-19 cases in Northern Italy, the department was designated as a dedicated center for hospitalized patients with suspected or confirmed COVID-19 in ordinary wards, physically separate from the main hospital. The department normally has 194 beds, with the capacity to expand to 330 when demand rises. Patient triage and admission pathways were specifically organized around this department to manage the pandemic, as described previously [4].

Adults (≥18 years) presenting to the Emergency Department with suspected COVID-19—manifesting as fever, cough, dyspnea, diarrhea, or known exposure to confirmed cases—underwent chest imaging, primarily high-resolution computed tomography (HRCT), in a dedicated unit. Patients whose imaging and clinical presentation suggested interstitial pneumonia were admitted to the Geriatric-Rehabilitation Department, regardless of age or pre-existing conditions, and nasopharyngeal swabs were collected for SARS-CoV-2 RT-PCR testing [4]. During the pandemic peak, these patients were considered at high probability for COVID-19 based on symptoms, exposure history, and radiologic findings.

Chest HRCT scans were evaluated by radiologists experienced in thoracic imaging. A scan was considered compatible with COVID-19 if it showed ground-glass opacities, either alone or in combination with consolidations, nodular or mass-like lesions, organizing patterns, perilobular opacification, or the reverse-halo sign [22, 23]. These criteria align with international recommendations for COVID-19 imaging [24]. Other findings sometimes observed in COVID-19, such as pulmonary vessel enlargement, subpleural lines, dependent atelectasis, pleural or pericardial effusions, and mediastinal lymphadenopathy, were not used as diagnostic criteria [25].

The study included patients aged 18 years or older who exhibited both clinical symptoms and HRCT evidence of interstitial pneumonia. Individuals who did not receive HRCT on admission or lacked signs of interstitial pneumonia were excluded. The study protocol was approved by the local Ethics Committee (ID 273/2020/OSS/AOUPR). Written informed consent was obtained whenever feasible, in accordance with Italian regulations for retrospective studies.

Data collection

For each patient, demographic data, comorbidities, symptom onset and duration, vital signs at ED arrival and ward admission, imaging, laboratory results, and clinical course were collected from medical records. A set of 23 predefined comorbidities—including hypertension, diabetes, obesity, heart failure, CKD, COPD, asthma, prior stroke, parkinsonism, dementia, epilepsy, and malignancies—was recorded. Additionally, any chronic condition causing long-term disability, significant impact on quality of life, or requiring ongoing treatment was included in the total comorbidity count [26]. The CHA2DS2-VASc score was calculated as a measure of cardiometabolic multimorbidity [27], and the number of chronic medications used prior to admission was documented.

Functional dependency in activities of daily living, partial or complete, was retrieved from medical records and used as a surrogate marker for frailty and disability, following recommended approaches for retrospective studies [28].

HRCT findings at admission were recorded, including the presence of ground-glass opacities, consolidations, and the

COVID-19 visual score, which quantifies the percentage of lung parenchyma affected by interstitial changes. The score was calculated by experienced radiologists using standardized methods described previously [29].

Laboratory tests collected at admission included nasopharyngeal RT-PCR for SARS-CoV-2, arterial blood gases, complete blood count, creatinine, urea, electrolytes, bilirubin, AST, LDH, CPK, CRP, fibrinogen, and INR. Oxygen flow rates at the time of blood sampling were noted to calculate the PaO2/FiO2 ratio.

Clinical course was evaluated by hospital length of stay, maximum body temperature, lowest oxygen saturation, worst PaO2/FiO2 ratio, requirement for non-invasive ventilation, and ICU transfer. Final outcomes (death or discharge) were recorded. Medications administered for COVID-19 during hospitalization—including antivirals, antibiotics, hydroxychloroquine, enoxaparin, and corticosteroids—along with their duration, were also documented for each patient.

Statistical analysis

Data were summarized using medians and interquartile ranges (IQR) for continuous variables and percentages for categorical variables. To examine temporal patterns, patients were divided according to admission period: those admitted during the ascending phase of the pandemic (28 February–22 March 2020) and those admitted during the plateau and descending phases (23 March–10 June 2020). Initial comparisons between groups were performed using Mann–Whitney tests for continuous variables and chi-square tests for categorical variables. To account for potential confounding by age and sex, linear regression models were applied to continuous variables and binary logistic regression to categorical outcomes.

Further analyses explored differences based on age categories (≤70 years vs. >70 years), initial RT-PCR results for SARS-CoV-2 (positive vs. negative), multimorbidity (defined as ≥2 chronic conditions [26]), and functional status, categorized as independent, partially dependent, or fully dependent in daily activities. Comparisons were also conducted between patients who died during hospitalization and those who were discharged alive or transferred. Chi-square, Mann–Whitney, linear regression, and logistic regression were applied as appropriate.

To identify independent predictors of in-hospital mortality, stepwise multivariate logistic regression with forward selection was performed for the entire cohort (Model 1). To reduce the risk of selection bias, separate forward-selection logistic regression models were conducted for patients with positive and negative RT-PCR results (Models 2 and 3). Analyses were performed using SPSS v.26 (IBM, Armonk, NY, USA), with statistical significance set at $p < 0.05$.

Results

Temporal trends

Between 28 February and 10 June 2020, a total of 1,634 patients were admitted through the COVID-19 care pathway. After reviewing 1,487 medical records for eligibility, 1,264 patients (711 males, 553 females; aged 20–99 years) met inclusion criteria, all showing clinical and radiological evidence of COVID-19-related pneumonia.

Of these, 713 patients (56.4%; 435 males, 278 females) were admitted during the first, ascending phase of the pandemic wave, whereas 551 patients (276 males, 275 females) were admitted during the second, plateau-to-descending phase. Supplementary Figure S1 displays the age distribution for each phase. Key demographic, clinical, medical history, and laboratory parameters at admission for the two periods are summarized in **Table 1**.

Table 1. Comparison of the demographic, anamnestic, clinical features, and outcomes of patients hospitalized during different periods of the pandemic peak

	First Period of Pandemic Peak (28 February–22 March 2020) (n = 713)	Second Period of Pandemic Peak (23 March–10 June 2020) (n = 551)	p	p[a]
Demography				
Age, years	71 (60–80)	79 (66–86)	**<0.001**	-
Female gender	278 (39)	275 (50)	**<0.001**	-
Weight, kg	80 (69–91)	74 (63–86)	**<0.001**	0.078
Comorbidities and functional performance				
Chronic comorbidities, number	2 (1–4)	3 (2–5)	**<0.001**	**<0.001**
CHA_2DS_2Vasc score	2 (1–4)	3 (2–4)	**<0.001**	0.472
Hypertension	406 (57)	336 (61)	0.174	0.472
Diabetes	142 (20)	121 (22)	0.389	0.915
Heart disease	150 (21)	160 (29)	**0.002**	0.402
Obesity	93 (13)	61 (11)	0.297	0.944
Cancer	85 (12)	110 (20)	**<0.001**	**0.010**
COPD	64 (9)	66 (12)	0.141	0.624

Dementia	64 (9)	121 (22)	**<0.001**	**0.005**
Systemic drugs, n	3 (1–6)	4 (2–7)	**<0.001**	**0.013**
Complete autonomy in daily activities	520 (73)	275 (50)	**<0.001**	**<0.001**
Complete dependency in daily activities	64 (9)	149 (27)	**<0.001**	**<0.001**
Clinical presentation of suspect COVID-19				
Symptom duration, days	7 (4–10)	7 (3–10)	0.160	**0.025**
Cough	383 (54)	202 (37)	**<0.001**	**<0.001**
Dyspnea	335 (47)	325 (59)	**<0.001**	**0.025**
Fever	627 (88)	413 (75)	**<0.001**	**<0.001**
Diarrhea	43 (6)	44 (8)	0.210	0.271
Other symptoms	114 (16)	105 (19)	0.161	0.095
O_2 saturation in room air on triage, %	90 (89–91)	91 (91–92)	0.645	**0.048**
Temperature on admission, °C	37.0 (36.0–37.7)	36.0 (36.0–37.2)	**<0.001**	**<0.001**
O_2 flows administered on admission, %	30 (21–60)	36 (21–70)	**0.019**	0.987
CT visual score, %	30 (20–50)	30 (20–50)	0.739	0.235
Consolidations on chest CT	499 (70)	413 (75)	0.083	0.081
RT-PCR positive on admission	535 (75)	298 (54)	**<0.001**	**<0.001**
Outcome				
Intensive care unit	43 (6)	11 (2)	**0.020**	**0.023**
Death	195 (27)	123 (22)	**<0.001**	**<0.001**

[a]p adjusted for age and sex with linear or binary logistic regression. Data are shown as median and interquartile range or numbers and percentages. Crude comparisons were made with Mann-–Whitney test or chi-square test, as appropriate. p values <0.05 are indicated in bold.

During the second phase of the pandemic, hospitalized patients were notably older, with a median age of 79 years (IQR 66–86) compared to 71 years (IQR 60–80) in the first phase ($p < 0.001$), and a higher proportion were female (50% versus 39 percent, $p < 0.001$). Functional dependency was more prevalent in this group (27 percent vs. 9 percent, $p < 0.001$), alongside a greater accumulation of chronic conditions (median of 3 comorbidities, IQR 2–5 vs. 2, IQR 1–4; age- and sex-adjusted $p < 0.001$) and higher rates of polypharmacy (median 4 medications, IQR 2–7 vs. 3, IQR 1–6; age- and sex-adjusted $p < 0.001$). Symptom profiles also shifted, with fever and cough occurring less frequently, while dyspnea became more common in second-phase admissions. Despite similar durations of symptoms and comparable chest HRCT visual scores, these patients exhibited better oxygenation (PaO2/FiO2), fewer positive RT-PCR results for SARS-CoV-2 **(Table 1)**, and distinct patterns of laboratory abnormalities upon ward admission **(Table 2)**.

Table 2. Comparison of the main laboratory findings on hospital admission of patients during different periods of the pandemic peak

	First Period of Pandemic Peak (28 February–22 March 2020) (n = 713)	**Second Period of Pandemic Peak (23 March–10 June 2020) (n = 551)**	**p**	**p[a]**
Arterial blood gas analysis				
pH	7.45 (7.42–7.48)	7.44 (7.41–7.47)	**0.003**	0.169
HCO_3^-, mmol/L	25 (23–27)	25 (23–27)	0.064	0.824
pCO_2, mmHg	36 (32–39)	36 (33–40)	0.089	0.623
pO_2, mmHg	70 (59–85)	83 (68–106)	**<0.001**	**<0.001**
PaO_2/FiO_2, mmHg	238 (126–327)	268 (174–361)	**<0.001**	**<0.001**
Clinical chemistry and hematology				
Hemoglobin, g/dL	13.7 (12.5–14.8)	12.9 (11.4–14.2)	**<0.001**	**<0.001**
White Blood Cells, 1×10^9/L	6.41 (4.81–8.97)	7.15 (5.21–9.65)	**0.001**	**<0.001**
Lymphocytes, 1×10^9/L	0.90 (0.63–1.21)	0.91 (0.61–1.30)	0.385	**0.018**
Platelets, 1×10^9/L	201 (161–257)	220 (166–282)	**0.002**	**0.006**
Creatinine, mg/dL	0.9 (0.7–1.1)	0.9 (0.7–1.2)	0.889	0.272
Sodium, mEq/L	137 (135–140)	138 (135–140)	0.050	0.084
Potassium, mEq/L	4.0 (3.7–4.3)	4.0 (3.6–4.4)	0.304	0.469
Total bilirubin, mg/dL	0.7 (0.5–0.9)	0.7 (0.5–0.9)	0.090	0.916
Creatine-phosphokinase, IU/L	146 (82–363)	113 (57–233)	**<0.001**	**0.029**
Lactate-dehydrogenase, IU/L	357 (280–485)	318 (248–423)	**<0.001**	**0.004**
Aspartate aminotransferase, IU/L	47 (34–73)	39 (27–60)	**<0.001**	**0.035**
D-Dimer, ng/mL	972 (629–1650)	1075 (631–2043)	0.096	0.711
INR ratio	1.21 (1.13–1.30)	1.22 (1.13–1.36)	0.120	0.059
aPTT ratio	0.96 (0.90–1.05)	0.98 (0.90–1.07)	**0.017**	0.205

Fibrinogen, mg/dL	629 (513–754)	580 (465–730)	**0.001**	**0.017**
C-reactive protein, mg/L	101 (52–167)	93 (39–154)	**0.039**	0.172

[a]p adjusted for age and sex with linear regression. Data are shown as median and interquartile range. Crude comparisons were made with Mann–Whitney test, as appropriate. p values <0.05 are indicated in bold.

Patients admitted during the second phase of the pandemic required less respiratory support, with a lower median maximum oxygen flow during hospitalization (36 percent, IQR 28–75 vs. 50 percent, IQR 28–75; age- and sex-adjusted $p < 0.001$), were less frequently treated with non-invasive mechanical ventilation (7 percent vs. 12 percent, $p = 0.003$), and experienced reduced in-hospital mortality (22 percent vs. 27 percent, $p < 0.001$) (**Table 1**, Supplementary Table S1). Additionally, the prescription patterns of medications used to treat COVID-19 differed between the first and second phases of the pandemic peak (Supplementary Table S1).

When comparing patients by age, those older than 70 years exhibited distinct clinical and anamnestic profiles relative to patients aged 70 or younger **(Table 3)**. Older individuals were more often female, carried a greater burden of chronic comorbidities, and had higher rates of functional dependency. Symptom patterns also differed, with fever and cough being less common and dyspnea more frequent, leading to lower room-air oxygen saturation and increased need for supplemental oxygen **(Table 3)**. These age-related differences were further reflected in laboratory findings: patients over 70 had lower PaO2/FiO2 ratios, hemoglobin, lymphocyte, and platelet counts, and elevated levels of creatinine, sodium, D-dimer, and CRP compared to younger patients (Supplementary Table S2).

Table 3. Comparison of the demographic, anamnestic, clinical features, and outcomes of patients hospitalized for suspect COVID-19, categorized by age (>70 years old vs. ≤70 years old)

	Age ≤ 70 N = 492	**Age > 70 N = 772**	**p**	**p[a]**
Demography				
Female gender	177 (36)	377 (49)	**<0.001**	
Weight, kg	84 (73–97)	72 (62–83)	**<0.001**	**0.001**
Comorbidities and functional performance				
Chronic comorbidities, number	2 (1–3)	3 (2–5)	**<0.001**	**<0.001**
CHA_2DS_2Vasc score	1 (0–2)	4 (3–5)	**<0.001**	**<0.001**
Hypertension	202 (41)	531 (69)	**<0.001**	**<0.001**
Diabetes	74 (15)	192 (25)	**<0.001**	**<0.001**
Heart disease	54 (11)	262 (34)	**<0.001**	**<0.001**
Obesity	93 (19)	54 (7)	**<0.001**	**<0.001**
Cancer	49 (10)	146 (19)	**<0.001**	**<0.001**
COPD	20 (4)	108 (14)	**<0.001**	**<0.001**
Dementia	5 (1)	177 (23)	**<0.001**	**<0.001**
Systemic drugs, n	2 (0–4)	5 (3–7)	**<0.001**	**<0.001**
Complete autonomy in daily activities	464 (95)	321 (42)	**<0.001**	**<0.001**
Complete dependency in daily activities	10 (2)	199 (26)	**<0.001**	**<0.001**
Clinical presentation of suspect COVID-19				
Symptom duration, days	7 (5–10)	7 (3–10)	**<0.001**	**0.001**
Cough	289 (59)	298 (39)	**<0.001**	**<0.001**
Dyspnea	225 (46)	435 (57)	**<0.001**	**<0.001**
Fever	446 (91)	588 (77)	**<0.001**	**<0.001**
Diarrhea	44 (9)	46 (6)	0.153	0.139
Other symptoms	74 (15)	145 (19)	0.062	0.081
O_2 saturation in room air on triage, %	94 (90–97)	92 (88–95)	**<0.001**	**<0.001**
Temperature on admission, °C	36.9 (36.0–37.8)	36.5 (36.0–37.4)	**<0.001**	**<0.001**
O_2 flows administered on admission, %	28 (21–44)	36 (21–75)	**<0.001**	**<0.001**
CT visual score, %	30 (20–45)	30 (20–50)	0.158	**0.029**
Consolidations on chest CT	334 (68)	522 (68)	0.810	0.594
RT-PCR positive on admission	310 (64)	499 (67)	0.279	0.187
Outcome				
Intensive care unit	49 (10)	8 (1)	**<0.001**	**<0.001**
Death	37 (8)	281 (36)	**<0.001**	**<0.001**

[a]p adjusted for sex with linear or binary logistic regression. Data are shown as median and interquartile range or numbers and percentages. Crude comparisons were made with Mann–Whitney test or chi-square test, as appropriate. p values <0.05 are indicated in bold.

Clinical features based on RT-PCR status at admission

Out of the total cohort, 807 patients tested positive for SARS-CoV-2 via nasopharyngeal swabs on the day of admission (468 males and 339 females). Conversely, 422 patients (229 males, 193 females) had negative RT-PCR results despite showing epidemiologic, clinical, and imaging features suggestive of COVID-19. For 35 patients, swabs were not performed on the admission day. When comparing these two groups (Supplementary Tables S3 and S4), RT-PCR negative patients, despite having similar HRCT patterns, displayed less frequent fever and generally required lower levels of oxygen supplementation. Their median PaO2/FiO2 was notably higher at 270 mmHg (IQR 206–362) compared to 236 mmHg (IQR 126–333) in the RT-PCR positive group, even after adjusting for age and sex ($p < 0.001$). Laboratory profiles also differed: negative patients had higher D-dimer and lymphocyte counts, while CRP levels were lower (Supplementary Table S4).

Effect of multimorbidity on clinical outcomes

Multimorbidity, defined as having at least two chronic conditions, was observed in 923 patients, accounting for 73% of the cohort. Its prevalence increased from 68% during the first phase to 81% in the second phase of the pandemic. Comparisons between patients with and without multimorbidity are summarized in **Table 4** and Supplementary Table S5. Those with multiple chronic conditions were older, more often female, and exhibited higher rates of functional dependency. While the presenting symptoms of COVID-19 did not differ markedly between groups, the disease course was more severe among multimorbid patients, with a significantly higher in-hospital mortality rate of 30% compared to 12% in non-multimorbid individuals (adjusted for age, sex, and period of admission; $p = 0.015$) (Supplementary Table S6).

Table 4. Comparison of the demographic, anamnestic and clinical features of patients categorized according to the presence of multimorbidity

	Patients without Multimorbidity (0–1 Chronic Diseases) (n = 335)	Patients with Multimorbidity (≥2 Chronic Diseases) (n = 923)	p	p[a]	p[b]	β Standardized or Odds Ratio (95% Confidence Interval) for Multimorbidity
Demography						
Age, years	61 (50–72)	78 (69–85)	**<0.001**	-	-	-
Female gender	117 (35)	434 (47)	**<0.001**	-	-	-
Weight, kg	80 (69–89)	75 (65–89)	0.135	**0.005**	**0.003**	0.120
Anamnestic data						
CHA_2DS_2Vasc score	1 (0–2)	3 (2–4)	**<0.001**	**<0.001**	**<0.001**	0.295
Systemic drugs, n	0 (0–1)	5 (3–7)	**<0.001**	**<0.001**	**<0.001**	0.468
Complete autonomy in daily activities	302 (90)	490 (53)	**<0.001**	**<0.001**	**<0.001**	0.30 (0.19–0.48)
Complete dependency in daily activities	10 (3)	203 (22)	**<0.001**	**<0.001**	**<0.001**	3.44 (1.67–7.11)
Clinical presentation of suspect COVID-19						
Symptom duration, days	7 (5–10)	7 (3–10)	**<0.001**	0.448	0.357	-
Cough	194 (58)	388 (42)	**<0.001**	0.133	0.227	-
Dyspnea	147 (44)	517 (56)	**<0.001**	0.295	0.396	-
Fever	302 (90)	738 (80)	**<0.001**	0.195	0.296	-
Diarrhea	27 (8)	64 (7)	0.264	0.779	0.694	-
Other symptoms	60 (18)	157 (17)	0.804	0.515	0.456	-
O_2 saturation in room air on triage, %	94 (90–97)	92 (88–95)	**<0.001**	0.462	0.571	-
Temperature on admission, °C	37.0 (36.0–37.8)	36.5 (36.0–37.5)	**<0.001**	**0.034**	0.086	-
O_2 flows administered on admission, %	28 (21–44)	35 (21–75)	**<0.001**	0.281	0.290	-
CT visual score, %	30 (20–40)	30 (20–50)	0.168	0.450	0.429	-

Consolidations on chest CT	228 (68)	627 (68)	0.896	0.992	0.963	-
RT-PCR positive on admission	211 (63)	618 (67)	0.198	0.153	**0.039**	1.38 (1.02–1.88)

[a]p adjusted for age and sex or [b] age, sex and period of admission with linear or binary logistic regression, as appropriate. Data are shown as median and interquartile range or numbers and percentages. Crude comparisons were made with Mann–Whitney or chi-square tests, as appropriate. Data on multimorbidity were available for 1258 of the 1264 patients included in the study. p values <0.05 are indicated in bold.

Impact of functional dependency in daily activities

Functional autonomy at the time of admission was recorded for 1,251 patients. Among these, 784 individuals (62.6%) were fully independent in daily activities, 257 (20.6%) had partial autonomy, and 210 (16.8%) were classified as disabled. Comparative analyses of admission characteristics, clinical course, and outcomes across these three groups are provided in Supplementary Tables S7–S9.

Patients with disability were generally older, predominantly female, and had a higher burden of chronic comorbidities (Supplementary Table S7). Their COVID-19 presentation featured a lower incidence of fever and cough but a higher prevalence of dyspnea. Notably, PaO2/FiO2 ratios at admission were similar across the three functional groups (Supplementary Table S7). In-hospital mortality rose progressively with decreasing functional autonomy: 17% among fully autonomous patients, 34% in those with partial autonomy, and 43% in disabled patients (p = 0.040, adjusted for age, sex, and admission period).

Determinants of adverse outcomes

Clinical and laboratory parameters at admission were further compared between patients who survived (discharged or transferred to other facilities) and those who died during hospitalization **(Tables 5 and 6)**. Patients who succumbed were older on average, had a greater number of comorbidities, and were more frequently functionally dependent. They also exhibited more extensive lung involvement on chest HRCT, with a median visual score of 45 (IQR 25–70) compared to 30 (IQR 15–40) in survivors (age- and sex-adjusted p < 0.001).

Respiratory function was markedly worse at admission among non-survivors, with a median PaO2/FiO2 ratio of 124 mmHg (IQR 79–242) versus 282 mmHg (IQR 200–366) in survivors (age- and sex-adjusted p < 0.001). Interestingly, the time from symptom onset to hospital presentation was slightly shorter in patients who died (median 6 days, IQR 3–8) compared with those who survived (median 7 days, IQR 4–10; age- and sex-adjusted p = 0.026) **(Tables 5 and 6)**.

Table 5. Comparison of the demographic, anamnestic, and clinical features of patients hospitalized for suspect COVID-19, categorized according to the outcome (discharged/transferred vs. dead during stay)

	Discharged or Transferred N = 946	**Dead during Stay N = 318**	**p**	**p[a]**
Demography				
Age	71 (59–81)	81 (75–87)	**<0.001**	-
Female gender	415 (44)	133 (42)	0.491	-
Weight, kg	78 (67–90)	73 (61–87)	**0.031**	0.732
Comorbidities and functional performance				
Chronic comorbidities, number	2 (1–4)	4 (2–5)	**<0.001**	**<0.001**
CHA_2DS_2Vasc score	2 (1–4)	4 (3–5)	**<0.001**	**<0.001**
Hypertension	519 (55)	219 (69)	**<0.001**	0.620
Diabetes	160 (17)	102 (32)	**<0.001**	**0.001**
Heart disease	198 (21)	118 (37)	**<0.001**	**0.046**
Obesity	113 (12)	35 (11)	0.756	0.089
Cancer	132 (14)	60 (19)	0.024	0.298
COPD	76 (8)	51 (16)	**<0.001**	0.145
Dementia	104 (11)	73 (18)	**<0.001**	0.198
Systemic drugs, n	3 (1–6)	5 (3–8)	**<0.001**	**0.001**
Complete autonomy in daily activities	647 (69)	139 (44)	**<0.001**	0.423
Complete dependency in daily activities	122 (13)	91 (29)	**<0.001**	**0.008**
Clinical presentation of suspect COVID-19				
Symptom duration, days	7 (4–10)	6 (3–8)	**<0.001**	**0.026**
Cough	470 (50)	116 (37)	**<0.001**	0.175
Dyspnea	460 (49)	201 (64)	**<0.001**	**0.004**
Fever	779 (83)	251 (80)	0.129	0.503
Diarrhea	75 (8)	13 (4)	**0.027**	0.098
Other symptoms	169 (18)	44 (14)	0.092	0.066

O_2 saturation in room air on triage, %	94 (90–96)	89 (80–93)	**<0.001**	**<0.001**
Temperature on admission, °C	36.6 (36.0–37.5)	36.6 (36.0–37.5)	0.757	0.248
O_2 flows administered on admission, %	28 (21–44)	75 (32–75)	**<0.001**	**<0.001**
CT visual score, %	30 (15–40)	45 (25–70)	**<0.001**	**<0.001**
Consolidations on chest CT	641 (68)	216 (68)	0.784	0.586
RT-PCR positive on admission	566 (61)	244 (81)	**<0.001**	**<0.001**

[a]p adjusted for sex and age with linear or binary logistic regression. Data are shown as median and interquartile range or numbers and percentages. Crude comparisons were made with Mann–Whitney test or chi-square test, as appropriate. p values <0.05 are indicated in bold.

Table 6. Comparison of the laboratory tests performed on admission of patients hospitalized for suspect COVID-19, categorized according to the outcome (discharged/transferred vs. dead during stay)

	Discharged or Transferred N = 946	**Dead during Stay N = 318**	**p**	**p[a]**
Arterial blood gas analysis				
pH	7.45 (7.42–7.47)	7.44 (7.40–7.48)	**0.002**	**<0.001**
HCO_3^-, mmol/L	25 (23–27)	24 (21–27)	**<0.001**	**<0.001**
pCO_2, mmHg	36 (33–40)	35 (31–38)	**0.001**	0.064
pO_2, mmHg	78 (66–95)	65 (54–83)	**<0.001**	**<0.001**
PaO_2/FiO_2, mmHg	282 (200–366)	124 (79–242)	**<0.001**	**<0.001**
Clinical chemistry and hematology				
Hemoglobin, g/dL	13.4 (12.2–14.5)	13.4 (11.5–13.4)	0.320	0.365
White Blood Cells, 1×10^9/L	6.54 (4.88–8.94)	7.37 (5.27–10.77)	**<0.001**	**<0.001**
Lymphocytes, 1×10^9/L	0.98 (0.70–1.33)	0.69 (0.46–1.00)	**<0.001**	**<0.001**
Platelets, 1×10^9/L	215 (169–273)	192 (150–245)	**<0.001**	**0.004**
Creatinine, mg/dL	0.9 (0.7–1.1)	1.1 (0.8–1.6)	**<0.001**	**<0.001**
Sodium, mEq/L	137 (135–139)	139 (135–142)	**<0.001**	**0.001**
Potassium, mEq/L	4.0 (3.7–4.3)	4.1 (3.7–4.5)	**0.005**	**0.010**
Total bilirubin, mg/dL	0.7 (0.5–0.9)	0.7 (0.5–1.0)	**0.006**	**0.018**
Creatine-phosphokinase, IU/L	125 (64–256)	170 (88–434)	**<0.001**	0.069
Lactate-dehydrogenase, IU/L	326 (256–416)	426 (300–610)	**<0.001**	**<0.001**
Aspartate aminotransferase, IU/L	41 (29–61)	55 (35–90)	**<0.001**	**<0.001**
D-Dimer, ng/mL	923 (607–1604)	1344 (854–3718)	**<0.001**	**<0.001**
INR ratio	1.21 (1.13–1.30)	1.23 (1.13–1.39)	**0.003**	0.099
aPTT ratio	0.97 (0.90–1.05)	0.99 (0.90–1.08)	**0.022**	0.969
Fibrinogen, mg/dL	596 (490–730)	612 (480–754)	0.737	0.801
C-reactive protein, mg/L	87 (37–141)	132 (74–206)	**<0.001**	**<0.001**

[a]p adjusted for sex and age with linear regression. Data are shown as median and interquartile range. Crude comparisons were made with Mann–Whitney test, as appropriate. p values <0.05 are indicated in bold.

Binary logistic regression models with forward-selection were applied to identify clinical and anamnestic factors independently associated with in-hospital mortality, as summarized in **Table 7**. Model 1 included the entire cohort of 1,264 patients. To address potential selection bias, Model 2 was restricted to patients who tested positive for SARS-CoV-2 by RT-PCR on their first nasopharyngeal swab during hospitalization (807 patients). Model 3 focused exclusively on patients with negative RT-PCR results at admission (422 patients) to determine predictors of mortality within this subgroup.

Table 7. Stepwise forward-selection logistic regression evaluating factors independently linked to hospital mortality. Model 1: all 1,264 study participants. Model 2: only patients with positive RT-PCR results on admission (807 patients). Model 3: only patients with negative RT-PCR results on admission (422 patients)

	Odds Ratio	**95% Confidence Interval**	**p[a]**
Model 1			
Age classes [b]	2.236	1.754–2.851	**<0.001**
PaO_2/FiO_2 on admission, mmHg	0.994	0.992–0.997	**<0.001**
RT-PCR test positive for SARS-CoV-2 on admission	2.877	1.640–5.047	**<0.001**
Admission after 3/23/2020	0.427	0.260–0.700	**0.001**
CT visual score, %	1.019	1.007–1.032	**0.003**
Lymphocyte count [c], 1×10^9/L	0.467	0.281–0.774	**0.003**
Platelet count [c], 1×10^9/L	0.996	0.993–0.999	**0.007**
Chronic diseases, number	1.166	1.036–1.313	**0.011**

Creatinine, mg/dL	1.291	1.045–1.595	**0.018**
Lactate dehydrogenase, IU/L	1.002	1.001–1.003	**0.023**
White Blood Cell count, 1 × 10^9/L	1.071	1.005–1.142	**0.035**
Total dependency in daily activities	1.927	1.027–3.618	**0.041**
Model 2			
Age classes [b]	2.356	1.799–3.086	**<0.001**
PaO_2/FiO_2 on admission, mmHg	0.993	0.990–0.996	**<0.001**
Lactate dehydrogenase, IU/L	1.002	1.001–1.004	**0.001**
Lymphocyte count [c], 1 × 10^9/L	0.481	0.286–0.809	**0.006**
Admission after 3/23/2020	0.512	0.302–0.869	**0.013**
Chronic diseases, number	1.173	1.031–1.335	**0.015**
Female sex	0.549	0.329–0.915	**0.021**
Model 3			
Age classes [b]	3.039	1.655–5.580	**<0.001**
CT visual score, %	1.052	1.021–1.084	**0.001**
PaO_2/FiO_2 on admission, mmHg	0.993	0.988–0.997	**0.003**
Creatinine, mg/dL	2.283	1.236–4.216	**0.008**
Platelet count [c], 1 × 10^9/L	0.993	0.988–0.999	**0.021**

[a] All remaining clinical, anamnestic, and laboratory variables that showed significant differences in unadjusted comparisons between patients who died during hospitalization and those who were discharged or transferred were included in the forward-selection logistic regression model.
[b] Age was categorized into the following groups: ≤55 years, 56–65 years, 66–75 years, 76–85 years, and >85 years.
[c] For these parameters, the reported odds ratios correspond to increments of 1,000 cells/μL. Values with $p < 0.05$ are highlighted in bold.

Age, the burden of chronic diseases, and functional dependency were all independently linked to higher likelihood of in-hospital death. In addition, indicators reflecting the severity of COVID-19, including PaO2/FiO2 at admission, platelet count, and serum LDH, were significant predictors. Notably, patients admitted during the second phase of the pandemic experienced lower mortality, both in the overall population (OR 0.427, 95% CI 0.260–0.700, p = 0.001) and among those testing positive for SARS-CoV-2 (OR 0.512, 95% CI 0.302–0.869, p = 0.013).

Discussion

This investigation offers a detailed snapshot of clinical characteristics and outcomes among a substantial cohort of patients hospitalized with suspected COVID-19 at a major Northern Italian academic hospital during the first wave (March–June 2020). The hospital's role as the primary COVID-19 hub for a large regional district provides a unique perspective on how the disease manifested across different phases of the pandemic.

Northern Italy's surge in COVID-19 cases compelled the government to enforce strict containment measures nationwide starting 10 March 2020 [2,30]. Since such interventions typically take 10–20 days to impact infection and hospitalization rates [31], patients admitted before 23 March were likely infected before lockdown, while those admitted afterward probably contracted the virus during the restrictions.

Our findings highlight clear differences between patients admitted in the early versus later phase. Those hospitalized during the second phase tended to be older, frailer, more often disabled, and carried a heavier burden of chronic illness. This pattern suggests a delayed infection timeline among older, multimorbid individuals compared with younger, healthier adults.

Confirming this observation will require further studies using broader community surveillance across larger regions. Nonetheless, these results underscore the importance of prioritizing preventive measures for older, frail, and multimorbid populations early in pandemic surges.

Interestingly, the second-phase patients displayed a somewhat distinct COVID-19 phenotype: fever and cough were less frequent, dyspnea was more common, PaO2/FiO2 levels on admission were higher, and laboratory abnormalities differed. Despite their older age and higher comorbidity, these patients experienced lower mortality.

Several factors may explain this trend. Improved community care may have refined patient selection for hospitalization, reducing admissions of less severe cases. Fewer new infections could have eased hospital burden, allowing better management. Additionally, clinicians' growing understanding of COVID-19 pathophysiology likely contributed to improved outcomes. The severe overcrowding during the initial weeks may have temporarily lowered standards of care, potentially worsening outcomes early in the outbreak [3].

The decline in mortality observed during the second phase of the pandemic may partly reflect the so-called "harvesting effect," in which individuals most vulnerable to SARS-CoV-2 are infected earlier and tend to exhibit more severe disease [32]. Nonetheless, the specific characteristics of patients admitted later make this explanation unlikely in our cohort.

Viral load likely also plays a role. Evidence indicates that SARS-CoV-2 concentrations in respiratory samples are higher in patients with severe disease compared with those

with milder forms [33-35]. In Italy, Clementi and colleagues reported that newly diagnosed patients at the end of the first wave had lower viral loads in nasopharyngeal swabs than patients diagnosed in the initial weeks of the outbreak [36]. These findings suggest that social distancing and lockdown measures may have reduced viral exposure. Our municipality observed similar trends in an unselected series of swabs [37].

Supporting this, the second phase of the pandemic showed a lower proportion of positive RT-PCR tests at hospital admission. Negative swabs in patients presenting with COVID-19-compatible symptoms and radiology, despite known exposure, have been documented previously [19, 38]. While these results may stem from sampling errors or inclusion of non-COVID interstitial pneumonia cases, they may also represent a distinct, low-inoculum phenotype characterized by reduced nasal viral shedding. Importantly, a negative RT-PCR result at admission does not exclude COVID-19, and in our data, these patients experienced lower mortality than those with immediate positive tests [39].

Our findings further underscore the impact of multimorbidity and frailty on COVID-19 outcomes. The clinical status at admission, particularly PaO2/FiO2 and laboratory markers such as platelet count and LDH, strongly influenced prognosis, consistent with studies in older populations [13, 40]. Frailty and multimorbidity, which frequently coexist and interact in older adults [41], shape the clinical phenotype and disease course, acting as additional risk factors for poor outcomes [13, 40], similar to other acute illnesses [42].

Previous studies have consistently shown that chronic conditions increase the risk of hospitalization and death from COVID-19 [7-10,43]. A multicenter Italian study identified diabetes, COPD, and chronic kidney disease as independent predictors of mortality [44], although overall comorbidity burden, measured by the Charlson Comorbidity Index, provided a stronger predictive value than individual diseases [44]. In line with this, our analysis demonstrated that the total number of chronic conditions, rather than any single comorbidity or the CHA2DS2Vasc score, was independently associated with hospital mortality.

Functional dependency—partial or total—also independently predicted mortality. Serving as a practical marker of frailty, these findings echo prior studies showing that the Clinical Frailty Scale reliably forecasts in-hospital death from COVID-19 [45-47], similar to other infections in elderly patients [48,49]. Nonetheless, the severity of COVID-19 at presentation appears to exert a stronger influence on outcomes than dependency alone, a conclusion supported by studies focused specifically on older hospitalized individuals [13, 50].

Several limitations must be acknowledged when interpreting our findings. First, the retrospective nature of this single-center study represents an inherent constraint. Selection bias cannot be entirely ruled out, as hospital admission dynamics during the COVID-19 peak may have been affected by local organizational factors. The fact that patients were admitted based on epidemiological, clinical, and radiological criteria rather than confirmed RT-PCR positivity introduces a potential source of bias, although, given the context of a pandemic wave, the pre-test probability of COVID-19 was very high in these cases. The exceptional emergency conditions and massive patient influx further represent potential limitations. Additionally, multimorbidity and frailty were evaluated using relatively coarse measures, as the crisis setting precluded comprehensive geriatric assessments. Finally, the small number of ICU transfers did not allow analysis of ICU admission as a secondary outcome.

Despite these limitations, several strengths support the robustness of our study. These include a large sample size, the designation of our department as the primary hub for suspected COVID-19 cases in a substantial geographic area, and the extensive dataset collected for each patient.

Conclusions

During the first COVID-19 wave in Northern Italy, we observed that older adults—particularly frail, multimorbid, and female patients—were more frequently hospitalized in the second phase of the outbreak and exhibited a distinct disease phenotype. These observations may inform targeted preventive strategies for older populations in future waves or similar outbreaks. While multimorbidity and dependency in daily activities were independently associated with in-hospital mortality, overall prognosis was largely determined by the COVID-19 phenotype, specifically the presence and severity of respiratory failure, as well as the timing of admission within the pandemic wave.

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