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The second wave of COVID-19 in Italy: a cohort study in a Respiratory Semi-Intensive Care Unit

La seconda ondata di COVID-19 in Italia: studio retrospettivo di coorte in una Terapia Semi-Intensiva Pneumologica

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Summary

Introduction. To face the second outbreak of COVID-19, our Respiratory Ward at Morgagni-Pierantoni General Hospital (Forlì FC, Italy) underwent a reorganization and a Respiratory Semi-Intensive Care Unit (RSICU) of 16 beds was created.

Material and methods. In this monocentric, retrospective, cohort study we report our experience in treating patients with moderate to severe acute respiratory failure due to COVID-19 infection.

Results. 108 patients were admitted to our RSICU between the beginning of October and 31st December 2020 and included in this study, with a median PaO_2/FiO_2 of 133.5 mmHg [IQR 85.8-170.8]. CPAP therapy was the most used support system (64.8%) and was associated with the lowest mortality (14.3%). NIV was provided to 29 patients (26.8%), with higher mortality (41.3%, n = 12) and intubation rates (n = 6) compared to the continuous positive airway pressure (CPAP) cohort. Only 10 (9.5%) patients out of 108 underwent intubation, 6 (60%) of whom died. Coronary hearth diseases (CHD) and hypertension were higher among non-survivor, while there was no significant difference for IL-6 and D-dimer levels and CT Severity Score.

Discussion. The use of non-invasive ventilation was correlated with need of intubation only in few patients with moderate to severe COVID-19 related acute hypoxemic respiratory failure (AHRF). CPAP therapy showed the best outcomes, with a mortality rate of 14.3% (n = 10). The histopathologic, CT and pathophysiological features of the L-phenotype suggest that in these COVID-19 patients, intubation and high PEEP might not be necessary for alveolar recruitment. Thus, a non-invasive approach can be appropriate, and this is consistent with our data. Pre-existing comorbidities might also affect the outcome of COVID-19.

Conclusions. Our findings indicate that non-invasive ventilation, particularly CPAP therapy is feasible and can be effective in treating in deteriorating COVID-19 patients, reducing the need for ICUs transferal.

Key words: COVID-19, AHRF, non-invasive mechanical ventilation, RSICU

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Conflict of interest statement
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Riassunto

Introduzione. *Al fine di affrontare la seconda ondata di COVID-19, il nostro reparto di Pneumologia all'Ospedale Morgagni-Pierantoni (Forlì FC, Italia) è stato riorganizzato ed è stata creata una Terapia Semi-Intensiva Pneumologica (UTSIP) a 16 letti.*

Materiali e metodi. *In questo studio di coorte retrospettivo e monocentrico riportiamo i dati della nostra esperienza nel trattamento dei pazienti con insufficienza respiratoria acuta (IRA) secondaria ad infezione da SARS-CoV-2.*

Risultati. *Fra l'inizio di ottobre e il 31 dicembre 2021 sono stati ricoverati nella nostra UTSIP 108 pazienti, con IRA ed un PaO_2/FiO_2 mediano di 133,5 mmHg [IQR 85,8-170,8]. La CPAP è stata il supporto respiratorio più usato (64,8%) e quello associato ad una minore mortalità (14,3%). La NIV è stata utilizzata in 29 pazienti (26,8%), con una mortalità del 41,3% (n = 12). Solo 10 pazienti sono stati intubati, 6 (60%) dei quali sono deceduti. L'ipertensione e la coronaropatia sono risultate essere le comorbilità più frequenti nel gruppo dei non-survivor. Non sono state riscontrate invece differenze significative di prevalenza per quanto concerne i livelli ematici di IL-6, D-dimero e gravità di estensione alla TC (TC Severity Score).*

Discussione. *L'uso della ventilazione non invasiva nella nostra UTSIP è stato associato ad una riduzione della necessità di trasferimento in Terapia Intensiva (TI) ed intubazione nei pazienti con IRA moderata-grave COVID-19 relata. Le caratteristiche istopatologiche e il quadro TC suggeriscono che in questi pazienti un'alta PEEP potrebbe non essere necessaria per il reclutamento alveolare, rendendo quindi preferibile un approccio non invasivo.*

Conclusioni. *La ventilazione non invasiva, in particolare la CPAP, eseguita in una UTSIP gestita da personale preparato è efficace nel trattare anche pazienti con un quadro di IRA avanzato, riducendo il bisogno di trasferimento in TI e l'intubazione.*

Parole chiave*: COVID-19, insufficienza respiratoria acuta, ventilazione meccanica non invasiva, UTSIP*

Introduction

Millions of COVID-19 cases have generated an unprecedented strain on health-care systems and increased the demand for Intensive Care Unit (ICU) beds [1]. At the beginning of COVID-19 pandemic, invasive mechanical ventilation (IMV) was recommended for patients with moderate to severe acute hypoxemic respiratory failure (AHRF) [2], also to prevent viral transmission [3]. However, early series reported high mortality for COVID-19 patients receiving IMV [4-6], raising the concern that these patients may be vulnerable to ventilator-induced lung injury.

The role of non-invasive supports was highlighted by Tobin et al. [7] and by other recent studies. Brusasco et al. [8] provided continuous positive airway pressure (CPAP) to patients presenting with severe intrapulmonary shunt (PaO_2/FiO_2 < 200 mmHg or PaO_2 < 60 mmHg on Ventimask 50%) or increased work of breathing (RR > 30/min or dyspnoea) and reported avoiding death or intubation in 36 out of 53 patients with PaO_2/FiO_2 < 150 and/or lung weight > 1.5 kg, which have been indicators for IMV in ARDS. Oranger at al. [9] described how CPAP can avoid intubation at 7 and 14 days, especially in patients with do-not-intubate order. Moreover, Franco et al. [10], in an observational study including 670 COVID-19 patients with PaO_2/FiO_2 of 152 ± 79 mmHg reported an overall unadjusted 30-day mortality rate of 26.9%, with 16%, 30% and 30% for HFNC, CPAP and NIV respectively.

To face the second outbreak of COVID-19, a Respiratory Semi-Intensive Care Unit (RSICU) was implemented in our Respiratory Ward at Morgagni-Pierantoni Hospital (Forlì, Italy) provided with 16 beds in negative pressure rooms. The aim of this study is to explore the outcomes of the patients admitted to RISCU and treated non-invasively and to assess the risk factors that could be related to in-hospital death.

Materials and methods

Study design and population

This was a monocentric, retrospective cohort study on consecutive patients with SARS-CoV-2 (RT-PCR test) related AHRF admitted to RSICU at Morgagni-Pierantoni General Hospital (Forlì FC, Italy) between 10th October and 31st December 2020. The study was approved by our local Ethic Committee (Prot. 1443/2021 I.5/29).

Patients' records were collected from electronic records system (Log80 System, Forlì-Italy). Data included: patients' demographic information, comorbidities, baseline laboratory tests (i.e., interleukine 6-IL6, LDH, blood glucose, ferritin, lymphocytes count, C reactive protein-CRP, estimated glomerular filtration rate-eGFR) and CT scan visual Severity Score (CT-SS). For each patient we reported the top respiratory support received. Humidified High Flow Nasal Cannula (HFNC) was delivered via AIRVO$_2$ (High Flow Nasal Cannula, Fisher&Paykel Healthcare). CPAP or non-invasive ventilation (NIV) were provided by turbine-driven mechanical ventilator (MonnalT75, Air Liquide Medical System Italia; Maquet Servo-Air, Getinge Group), air compressor ventilators (Siareton 4000 15", SIARE). CPAP was also delivered by flow generators (Bi-orespira or ventilator set in high flow mode) combined with Positive End-Expiratory Pressure (PEEP) valves. The interfaces were full-face or total-face masks and helmets (StarMed, Intersugical or DIMAR). Few patients received invasive mechanical ventilation (IMV) or oxygen through tracheostomy, because admitted to RSICU as a step-down unit from ICUs. Prone position was used according to clinical judgment, but not systematically registered and for this reason related data were not included.

Assessments

The severity of COVID-19 related AHRF was expressed

as the lowest PaO_2/FiO_2 ratio measured while on treatment with a PEEP > 5 cmH_2O or, in patients treated with HFNC, at the highest FiO_2. According to Berlin's criteria [11], hypoxemia was classified as mild if 200 mmHg < PaO_2/FiO_2 ≤ 300, moderate if 100 mmHg < PaO_2/FiO_2 ≤ 200 and severe if PaO_2/FiO_2 < 100 mmHg. A radiological severity score (CT-SS) was assigned by radiologists, ranging from 1 to 20 for each lung according to the number of regions involved and the intensity of opacity shown by CT scan pattern [12]. Four classes of severity of extension were identified: mild (CT-SS < 5/20); moderate (5 < CT-SS < 10), moderate-severe (10/20 < CT-SS < 15/20) and severe (CT-SS > 15/20).

Statistical analysis

The Shapiro-Wilk test was used to assess assumption of normality of continuous variables. Categorical variables are shown as frequency rates and percentages, and continuous variables as mean ± standard deviation (SD) or continuous variables were compared using independent groups' t-test when the data were normally distributed, otherwise, the Mann-Whitney test was used. Proportions for categorical variables were compared using Chi-square test or Fisher exact test. To explore the risk factors associated with in-hospital death, univariate and multivariate logistic regression models were used. We calculated unadjusted odds ratios (ORs) with 95% Confidence Intervals (95%CI) and p-values to select variables included in the multivariate logistic regression model. All covariates showed to be to be risk factors in the univariate analysis were included in multi-variated analysis. A two-sided α of less than 0.05 was considered statistically significant. Statistical analysis was performed with GraphPad Prism version 8.0.0 for Macintosh, GraphPad Software, San Diego, California USA, www.graphpad.com Regression models were perform using STATA software. StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.

Results

Demographic, clinical characteristics and laboratory tests

108 patients admitted to RSICU with a median PaO_2/FiO_2 ratio of 133.5 mmHg [IQR 85.8-170.8] were included into the analysis. Baseline characteristics are displayed in Table I.

Treatments

CPAP was delivered to 70 (64.8%) patients, with a median PaO_2/FiO_2 of 143 [IQR 111.5-175]. In the CPAP cohort 59 (84.3%) patients were treated non-invasively and discharged, 3 (4.3%) needed intubation and were transferred in ICUs. Mortality rate was 14.3% (n = 10): 8 patients died in RSICU, and 2 died intubated in ICUs. One was discharged from ICUs.

NIV was delivered to 29 (26.8%) patients, with a median PaO_2/FiO_2 ratio of 108 mmHg [IQR 66-147]. In NIV group, 14 (48.3%) patients were treated non-invasively and discharged, 7 (24.1%) needed intubation and were transferred in ICUs. Mortality rate was 41.3% (n = 12): 8 patients died in RSICU; 4 died intubated in ICUs. 3 patients were discharged from ICUs, HFNC as top support was used only for 7 (6.5%) patients. Median PaO_2/FiO_2 was 81 mmHg [IQR 80.5-167]. Mortality rate was 0.93% (n = 1) and nobody was admitted in the ICU.

Comparing patients treated with CPAP to those treated with NIV, we found that patients in the NIV cohort had more negative prognostic factors (Tab. III).

We included 108 patients, 84 (77.8%) survivors and 24 (22.2%) non-survivors, with complete data for the variables age (OR = 1.04, 95%CI 1-1.09), CHD, COPD, D-dimer level, blood glucose and e-GFR in the univariate analysis. The odds of in-hospital death were higher in older patients, in case of a severe hypoxia with PaO_2/FiO_2 < 100 mmHg (OR = 11.8, 95%CI 4.07-34.3) and for patients with pre-existing CHD (OR = 3.3, 95% 1.2-9.05), COPD (OR = 3.4, 95%CI 1.12-10.5) or diabetes mellitus (OR = 1.7, 95%CI 0.68-4.26). Higher baseline D-dimer (OR = 1.57, 95%CI 0.50-4.9) or blood glucose (OR = 1.3, 95%CI 0.72-5.2, and OR 2.27, 95%CI 0.57-9.0) and lower e-GFR (OR = 2.23, 95%CI 0.88-5.62) were also associated with increased risk. Intubation was associated with higher in-hospital death risk. A multivariate regression analysis, older age, lower PaO_2/FiO_2, intubation, CHD and COPD remained associated with death in patients with COVID-19 AHRF (Tab. IV).

Discussion

In this study, the use of non-invasive ventilation was correlated with need of intubation only in few patients with moderate to severe AHRF. CPAP was associated with best outcomes.

These results are in accordance with early series, which suggested high mortality for patients treated invasively. Richardson et al. 4 described mortality rates of 79.9% and 41.8%, for those who received IMV (18-to-65 years *vs* > 65 years respectively). According to data from Wuhan [5], 31 out of 32 patients (96.8%) treated with IMV died. Grasselli et al. [6] reported on 1591 patients hospitalized in the ICUs of Lombardy (Italy), with an overall mortality of 26%. In a retrospective multicentre study [13] including 1057 intubated patients in Italian ICUs mild, moderate, and severe ARDS were reported for 15, 50

Table I. Baseline demographic, clinical characteristics, and laboratory tests.

	Total N = 108	Survivors (N = 84)	Non-survivors (N = 24)	*p*-value
Age years, median [IQR]	71 [62.5-80]	69 [60-80]	77 [73.3-81]	0.032
Female, n (%)	30 (27.8)	24 (28.6)	6 (25%)	
PaO_2/FiO_2 mmHg, median [IQR]	133.5 [IQR 85.8-170.8]	150 [115-180]	70.5 [64.8-102]	< 0.0001
• PaO_2/FiO_2 > 200, n (%)	5 (6.54)	5 (5.95)	0	0.584
• PaO_2/FiO_2 100-200, n (%)	68 (62.9)	62 (73.8)	6 (25)	< 0.0001
• PaO_2/FiO_2 < 100, n (%)	35 (32.4)	17 (20.4)	18 (75)	< 0.0001
Hypertension, n (%)	65 (60.2)	47 (55.9)	18 (75)	0.104
Obesity, n (%)	43 (39.8)	31 (37)	12 (50)	0.344
CHD, n (%)	22 (23.4)	13 (15.5)	9 (41)	0.041
COPD, n (%)	16 (14.8)	9 (10.7)	7 (29.2)	0.045
Pulmonary fibrosis, n (%)	3 (2.7)	1 (1.2)	2 (8.3)	0.123
Cancer, n (%)	16 (14.8)	9 (10.7)	7 (29.2)	0.045
CKD, n (%)	24 (22.2)	17 (20.7)	7 (29.2)	0.122
Diabetes, n (%)	33 (30.6)	25 (29.7)	8 (33.3)	0.803
Lymphocytes/mmc median [IQR]	740 [487.5-1062.5]	735 [490-1085]	750 [417.5-915]	0.413
• Lymphopenia COVID-related (WBC< 1000/mmc), n (%)	76 (70.4)	56 (66.7)	20 (83.3)	0.135
CT Severity Score	N = 83	N = 68	N = 15	
• < 5/20 n (%)	4 (4.8)	4 (6)	0	> 0.999
• > 5 < 10/20 n (%)	27 (32.5)	20 (29)	7 (47)	0.234
• > 10 < 15/20 n (%)	34 (40.9)	30 (44)	4 (27)	0.253
• > 15/20 n (%)	18 (21.7)	14 (21)	4 (27)	0.731
D-dimer ug/L, median [IQR]	1084 [554.8-1881.5]	936.5 [549.5-1438.8]	1461 [110.8-4246.8]	0.014
Blood glucose, mg/dL median [IQR]	126.5 [106.8-179]	122 [102-175.5]	140.5 [117-211]	0.004
e-GFR ml/min, median [IQR]	76 [54-91]	82.5 [59-93]	56.5 [44.5-77.8]	0.008
• eGFR < 60 ml/min, n (%)	38 (35.2)	24 (30.9)	12 (50)	0.095
LDH U/L, median [IQR]	346 [280-402]	336 [270-404.5]	349 [291.5-387]	0.805
CRP mg/L, median [IQR]	107 [48-170]	106 [53-166]	120 [56.8-156]	0.652
IL-6 pg/mL, median [IQR]	102 [28-235]	94 [28-259]	117 [38-201]	0.684
Ferritin ng/mL, median [IQR]	771.5 [464.8-1283.8]	743.5 [534-1283]	947.5 [358-1271]	0.832

CHD: Coronary Heart Diseases; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; e-GFR: estimated Glomerular Filtration Rate; CRP: C-Reactive Protein; WBC: White Blood Cells.

and 35% of patients respectively, resulting in a mortality of 25,33 and 41%.

The histopathologic, CT and pathophysiological features of the L-phenotype suggest that in these COVID-19 patients, intubation and high PEEP might not be necessary for alveolar recruitment. Thus, a non-invasive approach can be appropriate, and this is consistent with our data.

Gattinoni et al. [14] suggested that, even meeting the ARDS Berlin criteria, several cases of COVID-19 pneumonia show a peculiar phenotype with not heavy-lungs and relatively preserved lung compliance despite severe hypoxemia (the so-called L phenotype). The studies by Doglioni et al. [15] and Chilosi et al. [16] may explain this phenotype. The histopathologic background of early COVID-19 is reported to be different from the diffuse alveolar damage seen in ARDS. Lung samples of early COVID-19 patients showed pristine alveolar structures, patchy type II pneumocytes hyperplasia, interstitial and perivenular infiltrates consisting mainly of CD4+ lymphocytes, intra-alveolar accumulation of "inflammatory" macrophages along with hyperplasia of inter-

Table II. Treatments.

	Total N = 108	Survivors (N = 84)	Non-survivors (N = 24)	*p*-value
CPAP, n (%)	70 (64.8)	60 (85.8)	10 (14.3)	0.333
NIV, n (%)	29 (26.8)	17 (58.6)	12 (41.4)	0.333
HFNC, n (%)	7 (6.5)	6 (85.7)	1 (14.3)	0.666
Oxygen via tracheostomy, n (%)	1 (0.93)	1 (100)	0	0.666
IMV via tracheostomy, n (%)	1 (0.93)	0	1 (100)	> 0.999
Intubated, n (%)	10 (9.3)	4 (40)	6 (60)	> 0.999

CPAP: Continuous Positive Airway Pressure; NIV: Non-Invasive Ventilation; HFNC: High Flow Nasal Cannula; IMV: Invasive Mechanical Ventilation.

Table III. CPAP group vs NIV group at baseline.

	CPAP (N = 70)	NIV (N = 29)	*p*-value
Age years, median [IQR]	71 [60-79]	74 [67-82]	0.117
PaO_2/FiO_2 mmHg, median [IQR]	143 [111.5-175]	108 [66-147]	0.008
Hypertension, n (%)	40 (57)	20 (68.9)	0.823
Obesity, n (%)	24 (343)	18 (62)	0.015
CHD, n (%)	13 (18.6)	9 (31)	0.192
COPD, n (%)	6 (8.6)	10 (34.5)	0.004
Pulmonary Fibrosis, n (%)	3 (4.3)	0 (0)	0.553
CKD, n (%)	14 (20)	7 (24.2)	0.787
Diabetes mellitus, n (%)	19 (27.2)	11 (37.9)	0.339
CT Severity Score	N = 60	N = 18	
• < 5/20, n (%)	3 (5)	0	0.553
• > 5 ≤ 10/20, n (%)	19 (31.7)	7 (38.9)	0.807
• > 10 ≤ 15/20, n (%)	28 (46.7)	3 (16.7)	0.004
• > 15/20, n (%)	10 (15.4)	8 (44.4)	0.153
Lymphocytes/mmc, median [IQR]	740 [490-1077]	720 [480-910]	0.588
• Lymphopenia COVID-related, n (%)	48 (68.6)	24 (82.7)	
D-dimer ug/L, median [IQR]	1077 [503-1946]	988.5 [612-1439.8]	0.903
Blood glucose mg/dL, median [IQR]	126.5 [106.8-165]	131 [111-181]	0.559
e-GRF ml/min, median [IQR]	77.5 [59.5-90.8	68 [39-91]	0.105
• eGFR < 60 ml/min, n (%)	22 (31.4)	13 (44.8)	
LDH U/L, median [IQR]	321 [270-391]	376 [283.8-438]	0.283
CRP mg/L, median [IQR]	101.5 [43.5-173.8]	123 [70-176.5]	0.986
IL-6 pg/mL, median [IQR]	63 [26.5-154.8]	216.5 [122.5-290]	0.601
Ferritin ng/mL, median [IQR]	862 [553-1394.5]	698.5 [409-1153]	0.197

CHD: Coronary Heart Diseases; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; e-GFR: Estimated Glomerular Filtration Rate; CRP: C-Reactive Protein.

alveolar capillaries and dilated post-capillary venules. Piciucchi et al. [17] suggested that intra-alveolar capillary changes might be the anatomic background of ground glass/crazy paving opacification, and along with the gravity dependent veins enlargement observed in CT scans (the "venoplegic/hyperaemic pattern"). Finally, Oldani et al. [18] suggested that the pathophysiology of the L-phenotype might be understood by the predominance of V/Q ratio inequality due to the neo-angiogenesis and the "vasoplegia" leading to blood overflow around almost pristine alveoli.

Several studies have reported the importance of comorbidities, particularly cardiovascular diseases, obesity, and diabetes in determining the severity of COVID-19

Table IV. Univariate and multivariate analysis.

	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age	1.04 (1-1.09)	0.034	1.09 (1.02-1-18)	0.014
PaO_2/FiO_2 mmHg				
• < 100 mmHg	11.8 (4.07-34.3)	< 0.001	8.96 (2.54-32-07)	0.001
Intubation present	6.66	0.006	12.69	0.018
• (*vs* non present)	(1.7-26.09)		(1.54-104.7)	
Comorbidity present (*vs* non present)				
• CHD	3.3 (1.2-9.05)	0.022	1.32 (0.31-5.55)	0.705
• COPD	3.4 (1.12-10.5)	0.031	1.47 (0.27-7.83)	0.653
• Diabetes mellitus	1.7 (0.68-4.26)	0.250		
Laboratory findings D-dimer, ug/L				
• > 500 < 1000	0.13 (0.14-1.22)	0.074		
• > 1000	1.57 (0.50-4.9)	0.440		
Blood glucose, mg/dL				
• 200 mg/dL	1.93 (0.72-5.2)	0.193		
• > 300 mg/dL	2.27 (0.57-9.0)	0.243		
e-GFR mg/ml/min				
• < 60	2.23 (0.88-5.62)	0.089		

CHD: Coronary Heart Diseases; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; e-GFR: Estimated Glomerular Filtration Rate; CRP: C-Reactive Protein.

illness [19,20]. In our cohort, the most common comorbidities were hypertension (60.2%), obesity (39.8%) and diabetes (30.6%). Nevertheless, there was no significant difference in prevalence for each of these between survivors and non-survivors. Blood glucose was higher among non-survivors ($p = 0.004$), but this result may be biased by the need for higher doses of corticosteroid used to treat severe patients (usually 80 mg/qd of methyl prednisolone for patients with $PaO_2/FiO_2 < 200$ mmHg) [21]. CKD was described in only 22.2% of patients, but baseline laboratory tests revealed moderate to severe kidney impairment (i.e., e-GFR < 60 mL/min/kg according to CKD-EPI formula) [22] in 38 patients (35.2%), significantly worse in non-survivors ($p = 0.008$). Kidney function abnormalities and acute kidney injury (AKI) seem hereby to be significatively associated with COVID-19 severity and outcomes. Hirsh et al. [23] found that AKI was a common among patients hospitalized with COVID-19 (36.6%). In another cohort [24] the authors described a high (76%) incidence of AKI, and an increased risk of death associated with AKI itself. The main respiratory comorbidity was COPD, followed by pulmonary fibrosis, which seem to be associated with higher risk of death, aligning with other studies [25,26].

Despite CT-SS was reported to correlate with inflammatory laboratory markers, oxygen requirement and to be a predictor of mortality [27,28], we did not report a significant difference between survivors and non-survivors (Tab. I).

Many authors have found a correlation between increased inflammatory indicators and COVID-19 severity. Gong et al. [29] stated that patients with severe disease have high levels of IL-6 (> 100 pg/mL). Coomes et al. [30] performed a meta-analysis of 16 papers: all patients had risen level of IL-6. In our study, inflammatory markers were elevated in the whole cohort, with higher level of IL-6 and CRP in non-survivors, although the differences were not statistically significant.

Lastly, coagulation abnormalities appear to be a common finding in COVID-19 patients. In a prospective observational study conducted in Italy [13], the authors found that the ventilatory ratio was higher in patients with elevated D-dimer irrespective of the patients' static compliance, suggesting that coagulopathy plays a role in increasing dead space. In our study we found a spread in D-dimer levels in the whole cohort, associated with other laboratory abnormalities compatible with coagulopathies, such as risen LDH and ferritin, but the univariate and multivariate analysis

did not confirm the increased risk of in-hospital mortality (Tab. III).

Our study has several limitations. It is a retrospective study, biased by its nature. Data collection was partial, especially for patients admitted from other wards, and for this reason time from admission to discharge, to intubation or death and sedative usage were not analyzed. A prospective, multicentric study with a control group is needed to better inform our results.

Conclusions

This study reports the real-life experience of our RSICU and confirms how non-invasive respiratory supports in this setting are effective to treat patients with moderate and severe COVID-19 related AHRF, reducing the need for ICUs transferral. Finally, we report that basal blood test, particularly D-dimer and IL-6, and CT-SS do not always predict outcomes.

Final considerations

1. The rapid onset of COVID-19 emergency has put healthcare systems under enormous pressure and from both an organizational and clinical point, requiring the creation of more ICUs beds and new Semi-Intensive Care Unit.
2. The use of non-invasive ventilation can lower the need for intubation also in patients with moderate to severe AHRF due to COVID-19 pneumoniae.
3. Our study support previous works that showed how more severe radiological involvement or blood gas impairment do not require mandatory invasive treatment.

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Serena Bensai and Stefano Oldani conceived the paper and equally contributed to write the draft down. Lara Bertolovic, Cristiano Colinelli, Siro Simoncelli, Corrado Ghirotti, Vanni Agnoletti, Luca Mezzatesta, Marina Terzitta, Stefano Maitan helped to collect the data and to interprete the results. Giorgia Valpiani analysed data and helped to interpret the results. Venerino Poletti contributed to the inception of the paper, reviewed it critically and supervised all the aspects of this paper.

Ethical disclosure

All patients involved consented their clinical data to be used for this paper.

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