COVID-19 and seasonal influenza infection outcomes in the ICU: a retrospective comparison study

M. TOCUT^{1,5}, M. SCHAMROTH PRAVDA^{2,5}, E. ILGIYAEV^{3,5}, Z. ROSMAN^{2,5}, N. SCHAMROTH PRAVDA^{4,5}, A. SOROKSKY^{2,5}

¹Department of Medicine C, ²Intensive Care Unit, Wolfson Medical Center, Holon, Israel

³Departments of Intensive Care, Sackler Faculty of Medicine and Shamir (Assaf Harofeh) Medical Center, Tel Aviv University, Tel Aviv, Israel

⁴Department of Cardiology, Rabin Medical Center, Petah Tikva, Israel

⁵Faculty of Medicine, Tel-Aviv University, Israel

Abstract. - OBJECTIVE: To compare the characteristics and outcomes of critically ill patients admitted to the intensive care unit (ICU) due to COVID-19 or influenza- associated pneumonia.

PATIENTS AND METHODS: We conducted a two-center retrospective study on patients admitted to the ICU due to either COVID-19 associated pneumonia (CAP) or influenza-associated pneumonia (IAP). Baseline characteristics, therapy during hospitalization and clinical outcomes were assessed.

RESULTS: Our study included 86 patients admitted to the ICU. Twenty-four patients (28%) had IAP and 62 patients (72%) had CAP. Those with IAP had more comorbidities of cardiac disease (p=0.005) and chronic obstructive lung disease (p=0.03) compared to those with CAP. Non-invasive ventilation was used significantly more in patients with IAP (p=0.001). The use of neuromuscular blockade was significantly higher in CAP patients (p=0.001). CAP patients had less favourable ventilation parameters. PEEP was significantly higher in those with CAP on the first day of admission (p=0.002). There was no difference in mortality (p=0.61) between the groups.

CONCLUSIONS: Patients admission to the ICU with CAP had less comorbidity than those with IAP. Patients with CAP had poorer ventilatory parameters patterns, requiring more aggressive ventilation and ECMO support. The overall mortality did not differ significantly between the groups.

Key Words:

Influenza, COVID-19, Acute Respiratory Distress Syndrome, Pneumonia, Intensive care unit.

Introduction

The novel coronavirus, severe acute respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has spread rapidly across the world, causing an international pandemic. The clinical disease resulting from this virus, known as Coronavirus Disease-2019 (COVID-19) can cause severe respiratory disease, specifically associated with Acute Respiratory Distress Syndrome (ARDS)¹. This has overwhelmed ICU units worldwide and the impact of this disease on patient outcomes to date is an emerging issue.

COVID-19 shares many commonalities with other viral pneumonias, including the route of infection, the clinical respiratory presentation and high mortality rates associated with severe disease²single-centre study including patients with COVID-19 or FLU pneumonia admitted to the Intensive care Unit (ICU. Therefore, severe influenza pneumonia has been used as a comparison to COVID-19 associated pneumonia. As COVID-19 presents in undulating waves of disease compared to the seasonal nature of influenza, information about the disease and its course is vital not only for our understanding of the clinical course of severe disease but equally important in order to allow the medical fraternity to prepare for forthcoming outbreaks. The aim of our study was to compare the characteristics and outcomes of critically ill patients admitted to the intensive care unit (ICU) due to Coronavirus Disease-2019 (COVID-19) compared to those admitted due to influenza associated pneumonia (IAP).

Patients and Methods

We conducted a retrospective comparison study involving patients admitted to ICU due to either COVID-19 associated pneumonia (CAP) or influenza-associated pneumonia (IAP) at two Israeli medical centers, the Edith Wolfson Medical Center and Shamir Medical Center. This study was approved by the Institutional Review Board of both centers, according to the Declaration of Helsinki (approval number 0024-20-WOMC). Patient data was collected from the hospitals' database software Namer (SAP, version GUI CORE ECC 6.77.4, Germany) and ICU Metavision program (imd-soft, version 44.68, Israel). Assessed parameters included patient demographics, comorbidities, type of infection, need for vasopressors, need for noninvasive ventilation (NIV), the need of continuous positive airway pressure (CPAP), use of high flow nasal cannula (HFNC), mechanical ventilation (MV) or extracorporeal device use such as extracorporeal membrane oxygenation (ECMO). Complications such as ARDS, ventilator acquired pneumonia (VAP), acute kidney injury (AKI), cardiovascular complications, septic shock and death were also assessed. MV respiratory parameters were represented by peak inspiratory pressure (PIP), tidal volume (TV), positive end expiratory pressure (PEEP), driving pressure (DP), mechanical power (MP, calculated as MP= 0.098 x TV x (peak pressure - Delta Pressure/2) x respiratory rate), minute ventilation (MiV) and ideal body weight (IBW, calculated in Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet, Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet). Detailed information is available in Appendix. Clinical prediction tools were calculated in order to determine the mortality risk at the time of ICU admission such as the Acute Physiology and Chronic Health Evaluation (APACHE) II score, calculated on the first day of ICU admission and the Sequential Organ Failure Assessment (SOFA) score calculated on the first, third, seventh and 14th day of hospitalization. Patients' data and outcomes were monitored up to 21 days or to ICU discharge or death. Diagnosis of COVID-19 and Influenza infections were made by conducting real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assays of nasal and pharyngeal swabs. RT-PCR assays from lower respiratory tract aspirates were also used in available cases.

The primary end point of this study was to characterize the demographic and clinical features of patients hospitalized for IAP compared to patients with CAP. The secondary end points included assessing ventilatory parameters associated with IAP and CAP and assessing for variables associated with in-hospital mortality.

Statistical Analysis

Statistical analysis was performed with SPSS v26 (IBM Corp., Armonk, NY, USA). This study provided descriptive and inferential data. For descriptive purposes, data was presented as a number of cases (N) and percentages (%) for categorical variables. Mean \pm standard deviation (SD) or median (interguartile range) were shown for continuous variables. Since all variables were not normally distributed, they were reported as median and interguartile range (IQR). Categorical variables were compared between IAP patients and CAP patients using Chi-Square tests and Fisher's tests. Continuous variables were compared between the groups using the Mann-Whitney test. All statistical tests were two sided and a p < 0.05was considered statistically significant.

Results

A total of 86 adult patients were admitted to the ICU due to CAP or IAP between October 2019 and March 2021. This cohort consisted of 58 males (67%) with a median age of 62 years (IQR 49-71 years). Twenty-four patients (28%) had IAP (type A n=20, type B n=4) and 62 patients (72%) had CAP. Baseline characteristics are detailed in Table I. There was no significant difference in the groups in terms of sex, age, APACHE II or SOFA score. Patients with IAP had more comorbidities specifically that of cardiac disease (25% vs. 3%, p=0.005) and chronic obstructive lung disease (21% vs. 5%, p=0.03) compared to those with CAP. Other comorbidities were not significantly different between the groups. Both groups had a mean BMI of 30kg/m² indicating that they were obese. Patients who were pregnant or had organ transplantation were in the CAP group only. Patients' hospital medical therapy, morbidity and mortality are shown in Table II.

NIV was used more frequently in patients with IAP (58% vs. 21%, p=0.001). Neuromuscular blockage was mainly administered in patients with CAP (63% vs. 33%, p=0.001). There was no group difference in terms of renal outcomes, heart failure or shock. ECMO support was used in 21 cases (18 with CAP and 3 with IAP). There were no significant group differences regarding ECMO use (13% vs. 29%, p=0.10). The mean SOFA score during the hospitalization course did not differ between the groups at any timeline.

Characteristics	Influenza n=24	COVID-19 n=62	Total n=86	<i>p</i> -value
Male n (%)	19 (79)	39 (63)	58 (67)	- 0.14
Female n (%)	5 (21)	23 (37)	28 (33)	- 0.14
Age median (IQR)	61 (46-73)	63 (53-70)	62 (49-71)	0.55
Influenza infection type A	20			
Influenza infection type B	4			
Weight median kg (IQR)	80 (71-90)	80 (72-95)	80 (70-95)	0.98
BMI kg/m ² mean	30	30	30	0.72
APACHE II score (mean points)	21	18	19	0.29
Past medical history n (%)				
No disease	15 (63)	29 (47)	44 (51)	0.19
Cardiac disease	6 (25)	2 (3)	8 (9)	0.005
COPD	5 (21)	3 (5)	8 (9)	0.03
Other lung disease	3 (13)	4 (7)	7 (8)	0.39
CRF	3 (13)	3 (5)	6 (7)	0.34
Hematological disease	1 (4)	10 (16)	11 (13)	0.17
Autoimmune disease	1 (4)	5 (8)	6 (7)	0.67
Pregnancy	0	2 (3)	2 (2)	0.59
Organ transplantation	0	3 (5)	3 (4)	0.55

Table I. General patient characteristics on ICU admission.

IQR: interquartile range; COPD: chronic lung disease; CRF: chronic renal failure.

Characteristics	Influenza n=24	COVID-19 n= 62	Total n=86	<i>p</i> -value
NIV use (%)	14 (58)	13 (21)	27 (34)	0.001
HFNC use (%)	12 (50)	30 (48)	42 (49)	0.89
ECMO use (%)	3 (13)	18 (29)	21 (24)	0.10
VAP during ICU stay (%)	8 (33)	34 (55)	42 (49)	0.07
Tracheostomy (%)	4 (17)	11 (18)	15 (17)	1.00
Organ Failure during peak of dise	ase n (%)			
ARF	9 (38)	21 (34)	30 (35)	0.75
Need for RRT	4 (17)	7 (11)	11 (13)	0.72
Shock	17 (71)	46 (74)	63 (73)	0.75
Heart failure	2 (8)	2 (3)	4 (5)	0.57
Platelets <150,000 (per mcL)	12 (50)	19 (31)	31 (36)	0.09
Use of NO	8 (33)	31 (30)	39 (45)	0.16
Use of NMB	8 (33)	39 (63)	47 (55)	0.01
Use of prone position	1 (4)	10 (16)	11 (13)	0.17
SOFA score (mean point)				
Day 1	7	7	7	0.93
Day 3	7	7	7	0.80
Day 7	8	7	7	0.73
Day 14	8	8	8	0.41

Table II. Patient hospital treatment, morbidity and mortality during ICU stay.

ICU: intensive care unit; NIV: noninvasive ventilation; HFNC: high flow nasal cannula; ECMO: extracorporeal membrane oxygenation; VAP: ventilator acquired pneumonia; ARF:Acute Renal failure; RRT: renal replacement therapy; NO: nitric oxide; NMB: neuromuscular blocking agents; SOFA: sequential organ failure assessment.

Respiratoryparameter median (IQR)	Influenza n=24	COVID-19 n= 62	Total n=86	<i>p</i> -value
PO ₂ /FiO2 ratio mmHg				
Day 1	154 (94.78- 234.88) n=24	129 (91.91-180.50) n=62	94 (438.09-193.12) n=86	0.53
Day 3	177 (130.50-259.37) n=24	138 (100.80-178.75) n=61	145 (106.90- 201.25) n=85	0.007
Day 5	175 (148.90-273.75) n=21	123 (98.75-177.98) n=56	143 (107.16- 206.25) n=77	0.003
Day 7	177 (126.67-247.50) n=19	137 (94.08-188.75) n=48	145 (110.76- 195.23) n=67	0.01
Day 14	181 (131.42-249.37) n=10	140 (90.41-192.50) n=30	159 (102.92- 192.50) n=40	0.11
Day 21 or last day of ICU stay	192 (139.70-360.23) n=17	149 (70.17-221.46) n=38	165 (95.91- 247.50) n=55	0.02
PEEP cmH ₂ 0				
Day 1	8 (6.50-11.00) n=17	14 (10.00-15.00) n=42	12 (8.00-15.00) n=59	0.002
Day 3	10 (7. 00-13.00) n=17	12 (9.00-14.00) n=43	12 (8.00-14.00) n=60	0.32
Day 5	10 (6.00-14.00) n=17	12 (8.00-14.00) n=41	11 (8.00-14.00) n=58	0.19
Day 7	10 (8.00-12.00) n=13	12 (10.00-14.00) n=36	11 (10.00-14.00) n=49	0.29
Day 14	8 (7.00-12.50) n=10	10 (7.00-12.00) n=27	9 (7.00-12.00) n=37	0.52
Day 21 or last day of ICU stay	7 (5.00-10.00) n=9	10 (7.00-12.00) n=28	10 (6.00-12.00) n=39	0.11
TV/IBW				
Day 1	7 (4.65-8.46) n=17	7 (5.85-9.36) n=43	7 (5.55-9.27) n=60	0.22
Day 3	7 (5.91-9.60) n=17	7 (4.88-8.66) n=44	7 (5.54- 8.80) n=61	0.37
Day 5	8 (6.32-8.12) n=17	7 (4.68-8.47) n=42	7 (5.00-8.22) n=59	0.32
Day 7	7 (4.62-8.17) n=15	6 (4.56-7.64) n=39	6 (4.60- 7.65) n=54	0.87
Day 14	8 (6.27-8.78) n=10	5 (3.80-6.98) n=27	6 (4.03- 7.93) n=37	0.02
Day 21 or last day of ICU stay	8 (5.98-8.68) n=35	5 (0.42-6.92) n=11	6 (3.30.7.04) n=46	0.005
DP cmH ₂ O				
Day 1	16 (13.00-19.00) n=17	16 (12.00-17.00) n=43	16 (12.00-18.00) n=60	0.58
Day 3	16 (13.00-18.00) n=17	15 (12.00-19.00) n=44	15 (12.00-18.00) n=61	0.75
Day 5	16 (13.00-18.50) n=17	16 (12.00-18.00) n=43	16 (12.00-18.00) n=60	0.83
Day 7	17 (13.00-18.00) n=12	12 (15.00-19.00) n=39	16 (13.00-18.00) n=51	0.95
Day 14	15 (12.00-17.75) n=10	15 (12.00-20.00) n=27	15 (12.00-20.00) n=37	0.49
Day 21 or last day of ICU stay	15 (13.00-19.00) n=11	17 (12.00-21.00) n=29	16 (14.00-21.00) n=40	0.46

 Table III. Respiratory parameters during ICU stay.

Continued

Respiratoryparameter median (IQR)	Influenza n=24	COVID-19 n= 62	Total n=86	<i>p</i> -value
МР				
Day 1	18,769 (12,515.38-29,782.20) n=17	22,444.69 (16,495.04- 32,050.99) n=44	21,244 (16,207.48-31,984.26) n=61	0.36
Day 3	23,896 (16,840.32-30,846.77) n=17	20,359.10 (13,847.10- 30,873.52) n=45	21,080 (15,229.05- 30,776.36) n=62	0.55
Day 5	16,321 (12,499.41-26,612.88) n=17	20,774.04 (14,179.62-31,252.92) n=42	20,405 (13,970.88- 28,806.92) n=59	0.33
Day 7	20,639 (13,280.17-25,248.72) n=13	18,899.30 (9,376.64-27,730.08) n=39	19,045 (10,411.52-25,672.32) n=52	0.92
Day 14	19,034 (16,392.85-26,991.55) n=10	17,066.70 (10,716.30-25,777.92) n=27	18,061 (12,524.40- 25,763.80) n=3 7	0.39
Day 21 or last day of ICU	15,312 (11,630.64-28,735.56) n=11	16,001 (3,418.63-31,587.06) n=21	15,476 (10,566.60- 30,698.01) n=32	0.59

Table III. Respiratory parameters during ICU stay.

IQR: intensive care unit; PEEP: positive end expiratory pressure; TV: tidal volume; IBW: ideal body weight; DP: driving pressure; MP: mechanical power.

Tables III, IV and V detail the respiratory parameters of the two patient groups. The following respiratory parameters were significantly less favourable amongst those with CAP: PO₂/FiO₂ ratio was significantly lower on day 3, 5, 7 and day 21/last day of ICU stay. PEEP was significantly higher on the first day of admission (14 cmH₂0 vs. 8 cmH₂O, p=0.002) but did not differ in com-

parison with IAP patients until hospital discharge. TV/IBW was significantly lower on day 14 and day 21/last day of ICU stay. The highest PEEP value during admission was significantly higher amongst those with CAP (16 cmH₂0 vs. 14 cm-H₂O, p=0.02).

There was no group difference when comparing mortality rates (37% vs. 44%, p=0.61).

Table IV. Worst ventilatory/respiratory parameters during ICU stay.

Respiratory parameter	Influenza	COVID-19	Total	<i>p</i> -value
median (IQR)	n=24	n= 62	n=86	
Highest PIP	34 (27.45-37.00)	39 (31.00-47.00)	37 (28.75-44.25)	0.14
cm H ₂ O	n=20	n=46	n=66	
Highest FiO2	80 (50.00-95.00)	93 (60.00-100.00)	86 (60.00-100.00)	0.07
%	n=23	n=62	n=85	
Lowest PO ₂	51 (34.00-66.00)	53 (47.00-58.00)	53 (44.00-60.00)	0.54
mmHg	n=24	n=62	n=86	
Lowest TV	166 (0.17-303.00)	119 (26.00-232.00)	132 (10.00-275.75)	0.68
ml	n=20	n=48	n=68	
Highest	14 (10.00-16.00)	16 (14.00-18.00)	15 (13.00-18.00)	0.02
PEEP cmH,0	n=19	n=47	n=66	
Highest MV	13 (9.00-14.00)	13 (10.00-20.00)	13 (10.00-17.00)	0.11
L per minute	n=20	n=48	n=68	
Highest PCO ₂	82 (63.25-100.00)	74 (56.00-95.00)	78 (59.00-98.00)	0.17
mmHg	n=24	n=62	n=86	
Lowest PH	7.21 (7.03-7.34) n=24	7.22 (7.09-7.36) n=62	7.22 (7.08-7.36) n=86	0.45
Highest DP	18 (16.00-20.00)	19 (12.00-16.00)	18 (16.00-22.00)	0.91
cmH ₂ O	n=17	n=47	n=64	
Highest MP	24,775 (20,320.50-33,879.02) n=17	33,192 (23,635.05-38,631.25) n=46	31,855 (21,269.06-37,664.10) n=64	0.09

IQR: interquartile range; PIP: peak inspiratory pressure; TV: tidal volume; PEE: positive end expiratory pressure; MV: minute ventilation; DP: driving pressure; MP: mechanical power.

Parameter median days (IQR)	Influenza n=24	COVID-19 n= 62	Total n= 86	<i>p</i> -value
Patients that survived n= 50				
ICU LOS	10 (5.00-21.00)	6 (12.00-24.00)	12 (6.00-23.00) n=50	0.62
Hospital LOS	17 (9.00-31.00)	24 (12.00-34.00)	24 (12.00-33.00) n=50	0.45
MV	5 (0.00-17.00)	7 (0.00-18.00)	6 (00.00-18.00) n=49	0.96
Ventilator free days	12 (00.00-21.00)	13 (0.75-20.00)	13 (0.25-19.00) n=32	0.82
NIV use mean days (SD +/-)	7 (+/-7)	1 (+/-1)	3 (+/-5)	< 0.005
HFNC use mean days (SD +/-)	2 (+/-2)	3 (+/-3)	3 (+/-2)	0.18
ECMO use mean days (SD +/-)	1 (+/- 4)	3 (+/-7)	3 (+/-6)	0.21
Patients who died n=36				
Died (%)	9 (37)	27 (44)	36 (42)	0.61
Hospital LOS	19 (13.00-34.50)	21 (17.00-32.00)	20 (16.00-32.00)	0.70
MV	12 (5.50-19.50)	14 (10.00-23.00)	14 (9.00-22.00)	0.45
Ventilator free days	0 (0.00-0.00)	13 (0.00-18.00)	1 (00.00-17.00)	0.001
NIV use mean days (SD +/-)	2 (+/-6)	0 (+/-1)	1 (+/-3)	0.46
HFNC use mean days (SD +/-)	1 (+/-2)	1 (+/-2)	1 (+/-2)	0.35
ECMO use mean days (SD +/-)	1 (+/- 2)	6 (+/-12)	5 (+/-11)	0.20

Table V. In hospital mortality of Influenza and COVID-19 patients comparing the use of mechanical ventilation, ICU, and hospital length of stay.

IQR: interquartile range; ICU: intensive care unit; LOS: length of stay; MV: mechanical ventilation; NIV: non-invasive ventilation; HFNC: high flow nasal cannula; ECMO: extracorporeal membrane oxygenation.

Amongst patients who died, patients with CAP had more significant ventilator free days than those with IAP (13 days *vs.* 0 days, p=0.001). Conversely, amongst patients that survived, IAP patients required more days with NIV use (7±7 days *vs.* 1±1 days, p < 0.005). Amongst the 18 patients CAP patients who received ECMO support 44% died during hospitalisation.

Discussion

The main objective of our study was to characterize the demographic and clinical features of patients hospitalized for IAP compared to CAP. Our findings from this retrospective study demonstrated the following: patients with IAP had more cardiac and respiratory comorbidities; they required more days of NIV use and had favorable respiratory parameters. CAP patients were administered more neuro-muscular blockage agents to improve the mechanical ventilation as has been shown in other studies ³. Mortality rates did not differ between the groups. Our results add to an increasing ongoing data pool that characterizes and compares Influenza and COVID-19 viral pneumonias^{4,5}. Ludwig et al⁶there is a discussion about the severity of coronavirus disease-2019 (COVID-19 reported that patients with COVID-19 had severe disease in terms of mortality, need of mechanical ventilation and ICU admission compared to patients with Influenza associated disease. However, in this study, specific demographic or clinical variable could not be attributed to explain the discrepancies between Influenza and COVID-19 clinical manifestations.

Data on IAP and CAP subgroup of patients is scarce and there are conflicting results regarding mortality and morbidity. A single center study from Italy did not find a difference in mortality rates when CAP and IAP patients were compared, which is similar to the findings of our study results. The Italian study also showed that IAP patients had significantly more chronic obstructive lung disease and chronic renal disease and they subsequently developed more invasive pulmonary aspergillosis compared to patients with CAP²single-centre study including patients with COVID-19 or FLU pneumonia admitted to the Intensive care Unit (ICU. In comparison, a multicenter study from France reported that CAP was associated with a higher risk of mortality with a 90-day mortality hazard ratio of 1.57, 95% CI [1.14-2.17], p=0.006. Interestingly, in addition, IAP patients died due to comorbidity related complications while patients with CAP had less comorbidity were more immunosuppressed and died from pulmonary sepsis. In this French study cohort, CAP patients had less severe disease as evaluated by lower SOFA scores compared to IAP patients⁷. Consecutive patients admitted to an ICU with SARS-CoV-2 pneumonia from 27 February to 4 April 2020 (COVID-19 group, which differs from our study findings where the SOFA score was similar between the two groups throughout the entire hospitalization period, and emphasizes that IAP and CAP clinical severity was similar and not a confounder.

The average BMI in our patients was 30 kg/m² which indicates that they were obese. This finding is of major importance due to multiple reasons. The incidence of ARDS increases in direct correlation with patients' BMI, and obese patients with a BMI>30 kg/m² are at higher risk of having respiratory complications with ARDS⁸. In addition, animal models have shown a correlation between obesity and predisposition to Influenza infection⁹. Furthermore, it has been suggested that obesity is a risk factor causing a low-grade inflammatory state and thus has a negative impact on the immune system by contributing to immune system dysregulation. Obesity has been shown to have a significant effect on COVID-19 disease progression, causing more severe disease in obese patients, resulting in a higher risk of mortality.

In COVID-19 disease, the lungs are the most commonly affected organ. The pathogenesis initially involves extensive alveolar injury and subsequent fibroproliferation¹⁰. This ventilator parameter findings in this study are consistent with the pathogenesis described, with initial poor arterial blood oxygenations during the acute destructive edematous phase followed by low lung compliance consistent with the fibrotic process^{11,12}. There is increasing evidence that the latter changes can be chronic and cause diffusion impairment and a restrictive ventilatory pattern¹³extent, and distribution of parenchymal changes in the lung after acute respiratory distress syndrome (ARDS. Our study is unique in that we explored multiple ventilator parameters when comparing IAP and CAP patients. We documented a pattern amongst patients with CAP. Firstly, these patients required higher PEEP on day 1. During the initial admission they had lower arterial blood oxygenation, and at the end of ICU hospitalization they had

lower TV/BMI parameters indicating lower lung compliance.

We also observed significantly higher rates of NIV use in Influenza patients, which might be explained by the aversion to use NIV during the COVID-19 pandemic in order to prevent respiratory COVID-19 transmission. Our cohort included 21 patients who needed ECMO support of which the majority were amongst those with CAP. The mortality amongst those with CAP and ECMO support was 44%. Less IAP patients (13%) needed ECMO support compared to more patients with CAP (29%) despite our clinical observation, due to our small cohort, statistical significance was not noted.

COVID-19 exposed the vulnerability of healthcare systems to pandemics. The importance of understanding the course of COVID-19 with the clinical manifestations of severe disease has resulted in the need to allow adequate resource allocations within the healthcare system. This is extremely important in the ICU setting in which there is limited bed availability and prolonged hospitalizations are necessary. Our study contributes to describing and clinically characterizing the patients with severe disease who were admitted to ICU with CAP and IAP and contributes to the knowledge of how to prepare for upcoming COVID-19 waves.

The main limitation of our study is the small sample size. This may have limited the ability in our analysis to detect further differences between the groups resulting in statistical significance. The retrospective nature of the study enabled us to create a common ventilator parameters protocol for IAP and CAP patients and then compare the final outcome. Furthermore, our study results are indicative of COVID-19 disease from SARS-CoV-2 of the variant delta, which may limit the applicability of our results to other coronavirus variants. Therefore, our results cannot be generalized to disease caused by other variants of the coronavirus.

Conclusions

CAP patients admitted to the ICU had less comorbidity than those with IAP. Mechanical ventilation parameters differed between CAP and IAP patients. CAP patients had poorer ventilation parameters requiring higher PEEP, more aggressive ventilation parameters and eventually a third required ECMO support. The ventilator parameters were consistent with the COVID-19 disease process and were not attributable to demographic or clinical characteristic.

Conflict of Interest

The authors declare no conflict of interest.

Ethics Committee Approval

This study was approved by the Institutional Review Board of both centers, according to the Declaration of Helsinki (approval number 0024-20-WOMC).

Informed Consent

Not applicable.

References

- Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Crit Care 2020; 24: 516.
- 2) Oliva A, Ceccarelli G, Borrazzo C, Ridolfi M, Ettorre GD, Alessandri F, Ruberto F, Pugliese F, Raponi GM, Russo A, Falletta A, Mastroianni CM, Venditti M. Comparison of clinical features and outcomes in COVID-19 and influenza pneumonia patients requiring intensive care unit admission. Infection 2021; 49: 965-975.
- Courcelle R, Gaudry S, Serck N, Blonz G, Lascarrou JB, Grimaldi D. Neuromuscular blocking agents (NMBA) for COVID-19 acute respiratory distress syndrome: a multicenter observational study. Crit Care 2020; 24: 446.
- Faust JS, Del Rio C. Assessment of deaths from COVID-19 and from seasonal influenza. JAMA Intern Med 2020; 180: 1045-1046.
- 5) Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: A

systematic review and meta-analysis of observational studies. Anaesthesia 2020; 75: 1340-1349.

- Ludwig M, Jacob J, Basedow F, Andersohn F, Walker J. Clinical outcomes and characteristics of patients hospitalized for Influenza or COVID-19 in Germany. Int J Infect Dis 2021; 103: 316-322.
- 7) De Marignan D, Vacheron CH, Ader F, Lecocq M, Richard JC, Frobert E, Casalegno JS, Couray-Targe S, Argaud L, Rimmele T, Aubrun F, Dailler F, Fellahi JL, Bohe J, Piriou V, Allaouchiche B, Friggeri A, Wallet F. A retrospective comparison of COVID-19 and seasonal influenza mortality and outcomes in the ICUs of a French university hospital. Eur J Anaesthesiol 2022; 39: 427-435.
- 8) Zhang W, Wang Y, Li W, Wang J. Association Between Obesity and Short-And Long-Term Mortality in Patients With Acute Respiratory Distress Syndrome Based on the Berlin Definition. Front Endocrinol (Lausanne) 2020; 11: 611435.
- Honce R, Wohlgemuth N, Meliopoulos VA, Short KR, Schultz-Cherry S. Influenza in high-risk hosts-lessons learned from animal models. Cold Spring Harb. Perspect Med 2020; 10: a038604.
- 10) Meduri GU. The role of the host defence response in the progression and outcome of ARDS: pathophysiological correlations and response to glucocorticoid treatment. Eur Respir J 1996; 9: 2650-2670.
- Marshall R, Bellingan G, Laurent G. The acute respiratory distress syndrome: fibrosis in the fast lane. Thorax 1998; 53: 815-817.
- Sweeney RM, McAuley DF. Acute respiratory distress syndrome. Lancet 2016; 388: 2416-2430.
- 13) Nöbauer-Huhmann IM, Eibenberger K, Schaefer-Prokop C, Steltzer H, Schlick W, Strasser K, Fridrich P, Herold CJ. Changes in lung parenchyma after acute respiratory distress syndrome (ARDS): Assessment with high-resolution computed tomography. Eur Radiol 2001; 11: 2436-2443.