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Coronavirus Pandemic

Early vs late ICU admission in patients with COVID-19 pneumonia

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Abstract

Introduction: The type of admission to the Intensive Care Unit (ICU) influences the prognosis of patients with severe pneumonia and, in the case of patients with COVID-19 pneumonia, this is still unexplored. The objective of this study was to determine the differences between early and late ICU admission.

Methodology: A retrospective cohort study of patients with COVID-19 pneumonia at two high-complexity hospitals in Colombia. Early ICU admission (EICUA) was defined as direct admission from the emergency department or within the first 24 hours of admission. Late ICU admission (LICUA) was defined as admission from the hospitalization service after 24 hours of arrival. A robust Cox regression was performed for the variable recovery time, to determine the impact of the ICU admission type in the hazard rate.

Results: 68.2% were EICUA patients and 31.8% were LICUA patients. Recovery and duration of hospital stay were significantly lower in EICUA than in LICUA (9 vs 15 days, $p = 0.0001$, and 10 vs 15.5 days, $p < 0.0001$, respectively). However, the duration of ICU stay (7 vs 9 days, $p = 0.131$) and the invasive mechanical ventilation requirement (48.9% vs 54.9%, $p = 0.374$) were not statistically significant. The 30-day follow-up showed no difference between the EICUA and LICUA (alive 97% vs 94.6%, $p = 0.705$).

Conclusions: Mortality between EICUA and LICUA patients with COVID-19 pneumonia showed no statistically significant differences. However, the recovery time, the probability intensity of instant recovery, and the duration of hospital stay were better in EICUA than in LICUA. Neither EICUA nor LICUA affects the final status (death) of patients.

Key words: COVID-19; pneumonia; intensive care unit admission; robust proportional hazard; recovery time.

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Introduction

Community-Acquired Pneumonia (CAP) ranks as the eighth leading cause of death in the United States, accounting for over one million hospital admissions annually. The overall hospital mortality rate for CAP is approximately 10%, but this figure escalates to 35%-58% among patients requiring Intensive Care Unit (ICU) admission, especially in elderly individuals with multiple comorbidities such as diabetes mellitus, malignancy, chronic obstructive pulmonary disease (COPD), and heart failure [1,2]. Notably, up to 36% of hospitalized CAP patients require ICU care, which is associated with significant morbidity, mortality, and increased healthcare costs. These admissions are frequently triggered by septic shock or respiratory failure [3,4].

At the end of 2019, the emergence of Coronavirus Disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), presented a global public health crisis. First identified in Wuhan, China, this novel pathogen rapidly led to severe pneumonia and hypoxemic respiratory failure, straining hospital and ICU resources worldwide [3,5-7]. Approximately 5% of COVID-19 patients who develop

respiratory failure require ICU admission, with associated mortality rates ranging from 30% to 80% [4-7].

While ICU admission provides intensive clinical monitoring and life support, the progression of the disease may continue despite optimal care. Moreover, ICU patients are at risk for nosocomial complications, including ventilator-associated pneumonia and device-associated bacteremia [7,8]. However, limited studies have investigated the clinical outcomes of CAP patients who are not admitted directly to the ICU. Our literature review revealed that the clinical differences between early and late ICU admission for patients with COVID-19 pneumonia remain unclear [3]. The primary objective of this study is to determine whether differences exist in mortality and recovery time between patients with COVID-19 pneumonia admitted early or late to the ICU.

Methodology

A retrospective cohort study was conducted, including all hospitalized patients with COVID-19 pneumonia admitted to the Intensive Care Units (ICU) of two high-complexity hospitals in Medellín, Colombia. Data were extracted from medical records, encompassing the entire patient population within the specified time frame, thereby eliminating the need for sample size calculation. Inclusion criteria were patients aged 18 and above with a confirmed diagnosis of COVID-19 pneumonia, verified either by a positive SARS-CoV-2 RT-PCR test following the Berlin protocol or by radiological diagnosis using chest X-rays or computed tomography. The study period extended from March 20 to December 31, 2020, at Clínica Medellín Grupo Quirónsalud (CMGQ) and Nueva Clínica Sagrado Corazón (NCSC). Patients admitted for palliative care or for conditions other than COVID-19 pneumonia were excluded.

Early ICU admission (EICUA) was defined as admission directly from the emergency department or within the first 24 hours of hospital arrival. Late ICU admission (LICUA) referred to admission from the hospitalization service after more than 24 hours of medical monitoring, during which standard medical therapy—including oxygen, corticosteroids, and low-molecular-weight heparin prophylaxis—was administered. This approach was based on the protocol proposed by Pinzón *et al.* [17,18]. LICUA patients were not admitted immediately due to the absence of imminent ventilatory failure. Post-discharge follow-up was conducted through outpatient consultations one month after discharge or via telephone.

A comprehensive dataset was compiled, including demographic variables, comorbidities, duration of symptoms at hospital admission, pharmacological treatments, presence of adult respiratory distress syndrome (ARDS), ICU stay duration, mechanical ventilation days, occurrences of secondary infections, dialysis, vasopressor requirements, vital signs, laboratory data, and chest imaging reports. Additionally, the CURB-65 Pneumonia score, the IDSA-ATS 2007 Pneumonia severity index, the National Early Warning Score (NEWS-2), and the Sequential Organ Failure Assessment (SOFA) score were assessed for all patients.

Statistical Analyses

Quantitative and qualitative variables were stratified based on the type of admission: EICUA and LICUA. For quantitative variables, sample medians along with their respective 95% bootstrap confidence intervals were calculated, and comparisons were made using a two-sided Mann-Whitney hypothesis test. Qualitative variables were reported as absolute frequencies with corresponding percentages and were compared using a two-sample Z-test for proportions.

To compare EICUA and LICUA patients, a robust Cox regression model [9] was employed to identify predictor variables influencing the hazard ratio (HR), thereby minimizing the potential impact of outlier observations. This model focused on the dependent variable "Recovery Time," defined as the number of days from hospital admission to ICU discharge. The decision to measure recovery time rather than time to death or failure was intentional, as both admission groups had a higher proportion of patients alive at the end of ICU care. The analysis aimed to assess the effect of admission type on the likelihood of requiring a longer duration for discharge.

The final statistical analysis involved a stepwise logistic regression for the dependent variable "Status," which was a binary indicator of whether the patient was alive or deceased following ICU care. This model considered qualitative predictor variables, including "Admission Type" (EICUA/LICUA), "Corticosteroid Use" (Yes/No), "Comorbidities" (Yes/No), "Sex" (Male/Female), and "Colchicine Use" (Yes/No). The primary goal was to determine whether the type of ICU admission influenced the discharge status of patients. All statistical analyses were performed using R statistical software [10-12].

Figure 1. Flowchart of patients with COVID-19 pneumonia admitted to ICU from March 30 to December 2020.

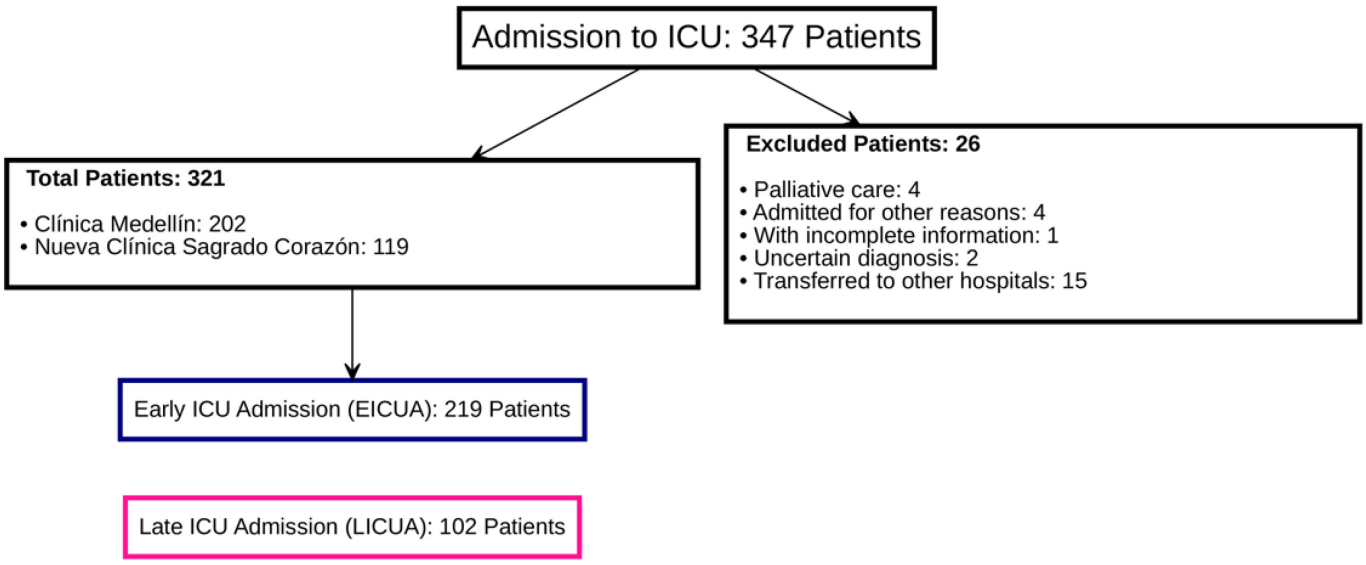


Table 1. Socio-demographic and clinical characteristics among patients with COVID-19 pneumonia, according to ICU admission type.

Variable	Admission-type		*p*
	EICUA (n = 219)	LICUA (n = 102)	
Age	61 (58-65)	62 (60-67)	0.494
Sex			
Male	147 (67.1%)	65 (63.7%)	0.637
Female	72 (32.9%)	37 (36.2%)	
Comorbidities	154 (70.3%)	78 (76.5%)	0.311
Cancer	17 (7.8%)	3 (2.9%)	0.157
Heart Disease	15 (6.8%)	14 (13.7%)	0.073
Renal Failure	24 (10.9%)	10 (9.8%)	0.906
Stroke	4 (1.8%)	1 (0.9%)	0.932
Obesity	64 (29.2%)	26 (25.5%)	0.576
COPD	24 (10.9%)	4 (3.9%)	0.062
Diabetes Mellitus	56 (25.6%)	25 (24.5%)	0.947
Hypertension	98 (44.7%)	61 (59.8%)	0.017
Symptoms Days	7 (7-8)	8 (7-8)	0.927
Initial ARDS			
Mild	45 (20.5%)	73 (71.6%)	< 0.0001
Moderate	56 (25.6%)	21 (20.6%)	0.404
Severe	117 (53.4%)	8 (7.8%)	< 0.0001
Unknown	1 (0.5%)	0 (0%)	1
Initial PaFi	92.5 (83-107)	239 (228-260)	< 0.0001
Initial C-Reactive Protein	16.6 (15-19)	13.6 (10.7-15.5)	< 0.0001
Initial Lactate Dehydrogenase	457.5 (423-480.9)	384 (334-429)	0.002
Initial Ferritin	873 (764-1000)	836 (633-996)	0.234
Initial D-Dimer	910 (788-1068)	738 (559-820)	0.025
History, Physical and Laboratory Data			
Hematocrit < 30%	11 (5%)	5 (4.9%)	1
Leukocytes < 4000	1 (0.5%)	5 (4.9%)	0.022
Blood Urea Nitrogen > 20	65 (29.7%)	33 (32.4%)	0.723
Sodium < 130	6 (2.7%)	4 (3.9%)	0.824
Breathing Freq. > 30	35 (15.9%)	3 (2.9%)	0.001
Systolic Blood Pressure < 90	4 (1.82%)	5 (4.9%)	0.234
Heart Rate > 125	11 (5%)	3 (2.9%)	0.578
Temperature > 38	25 (11.4%)	21 (20.6%)	0.044
Temperature < 36	9 (4.1%)	1 (0.9%)	0.247
Arterial pH < 7.35	12 (5.5%)	4 (3.9%)	0.748
SaO_2 < 90%	94 (42.9%)	42 (41.2%)	0.862

Results

A total of 321 patients were included in the study, with 219 classified as EICUA patients and 102 as LICUA patients (Figure 1). Statistical analyses revealed no significant differences between EICUA and LICUA patients overall, except for certain specific variables. Notably, significant differences were observed in the prevalence of hypertension (44.7% in EICUA vs. 59.8% in LICUA, $p = 0.017$) and the distribution of initial ARDS severity. EICUA patients had higher proportions of both mild (20.5% vs. 71.6%, $p < 0.0001$) and severe ARDS (53.4% vs. 7.8%, $p < 0.0001$).

Additional significant differences included PaFi (92.5 in EICUA vs. 239 in LICUA, $p < 0.0001$), C-Reactive Protein (CRP) levels (16.6 in EICUA vs. 13.6 in LICUA, $p < 0.0001$), lactate dehydrogenase (LDH) levels (457.5 in EICUA vs. 384 in LICUA, $p = 0.002$), D-Dimer levels (910 in EICUA vs. 738 in LICUA, $p = 0.025$), leukocyte counts below 4000 (0.5% in EICUA vs. 4.9% in LICUA, $p = 0.022$), breathing frequency above 30 (15.9% in EICUA vs. 2.9% in LICUA, $p = 0.001$), and temperature exceeding 38 °C (11.4% in EICUA vs. 20.6% in LICUA, $p = 0.044$) (Table 1). These findings suggest that patients in the LICUA group generally presented with less severe health conditions. Consequently, they did not require immediate ICU admission, unlike those who experienced further deterioration in the emergency department.

Clinical Outcome

In the LICUA group, a higher percentage of patients received both corticosteroids (79.4% vs. 35.6%, $p < 0.0001$) and colchicine (69.6% vs. 21%, $p < 0.0001$) prior to ICU admission compared to EICUA patients. Recovery time and hospital stay duration were significantly shorter for EICUA patients than for LICUA patients (9 days vs. 15 days, $p = 0.0001$; 10 days vs. 15.5 days, $p < 0.0001$, respectively). However, no significant differences were observed between the two groups in terms of ICU stay duration (7 days vs. 9 days, $p = 0.131$) or the requirement for invasive mechanical ventilation (48.9% vs. 54.9%, $p = 0.374$). Mortality rates were lower in the EICUA group compared to the LICUA group, though the difference was not statistically significant (38.4% vs. 45.1%, $p = 0.306$). Overall, the 30-day outcomes did not show significant differences between admission types (alive: 97% vs. 94.6%, $p = 0.705$; deceased: 0% vs. 3.6%, $p = 0.154$) (Table 2).

Admission-type Incidence in Recovery Time

A robust Cox regression analysis was conducted to assess the impact of clinical variables on the hazard rate function of "Recovery Time." The model included the explanatory variables "Admission Type" (EICUA/LICUA), "Colchicine" (Yes/No), "Sex" (Male/Female), "Comorbidities" (Yes/No), and "Corticosteroids" (Yes/No). Of these variables, only "Admission Type" was found to be significant in modeling the hazard rate function (HR = 0.524, $p = 0.001$) (Table 3). The baseline level for "Admission Type" was EICUA, with an estimated regression coefficient of -0.647. This coefficient indicates that LICUA patients experience a reduction in the hazard rate by 0.524 compared to EICUA patients.

Table 2. Clinical characteristics among patients with COVID-19 pneumonia, according to ICU admission type.

Variable	Admission-type		*p*
	EICUA (n = 219)	LICUA (n = 102)	
Corticosteroids Before ICU	78 (35.6%)	81 (79.4%)	< 0.0001
Dexamethasone	5 (6.4%)	17 (20.9%)	0.015
Methylprednisolone	67 (85.9%)	52 (64.2%)	0.003
Unknown	6 (7.7%)	12 (14.8%)	0.243
Colchicine Before ICU	46 (21%)	71 (69.6%)	< 0.0001
ARDS at ICU			
Mild	40 (18.3%)	8 (7.8%)	0.023
Moderate	52 (23.7%)	29 (28.4%)	0.446
Severe	126 (57.5%)	65 (63.7%)	0.352
Unknown	1 (0.5%)	0 (0%)	1
Over-infection	39 (17.8%)	28 (27.5%)	0.067
Invasive Mechanical Ventilation	107 (48.9%)	56 (54.9%)	0.374
Days of Mechanical Ventilation	12 (10-15)	13.5 (9-20)	0.457
Recovery Time (days)	9 (8-10)	15 (11-16.5)	0.0001
Hospital Stay-Time (days)	10 (9-12)	15.5 (14.5-17.5)	< 0.0001
ICU Stay-Time (days)	7 (6-9)	9 (7-11)	0.131
Mortality	84 (38.4%)	46 (45.1%)	0.306
30-day Status			
Alive	131 (97%)	53 (94.6%)	0.705
Death	0 (0%)	2 (3.6%)	0.154
Unknown	4 (2.9%)	1 (1.8%)	1

Table 3. Robust Cox regression for recovery time analysis.

Variable	Coef.	Exp (Coef)	S.E. (Coef)	*p*
Admission-type (0 – EICUA and 1 – LICUA)	-0.647	0.524	0.2	0.001
Colchicine (0 – Yes and 1 – No)	-0.077	0.926	0.253	0.762
Sex (0 – Male and 1 – Female)	-0.012	0.988	0.187	0.948
Comorbidities (0 – Yes and 1 – No)	0.334	1.397	0.203	0.099
Corticosteroids (0 – Yes and 1 – No)	0.196	1.217	0.23	0.393

Consequently, LICUA patients have a lower probability of immediate recovery or ICU discharge, suggesting a greater likelihood of requiring more days for recovery (Figure 2).

Mortality rates did not show significant differences between the two groups. A stepwise logistic regression model was employed to evaluate the influence of "Admission Type" on the response variable "Status." The best model, as determined by the Akaike Information Criterion (AIC), included only "Admission Type" and "Colchicine," yielding an AIC of 431.02 (Table 4). However, neither variable reached statistical significance (p = 0.079 and p = 0.142, respectively), indicating that "Admission Type" does not significantly impact or predict the final status of patients with COVID-19 pneumonia after ICU care.

Pneumonia Scores by admission-type

According to the NEWS-2 score, 75.8% of EICUA patients met the criteria for ICU surveillance (medium or high risk of deterioration), while only 50% of LICUA patients met these criteria. The IDSA-ATS score indicated that 58.9% of EICUA patients presented with initial criteria for severe pneumonia, compared to 35.3% of LICUA patients. In contrast, the CURB-65 score showed that 66% of EICUA patients did not meet the criteria for ICU admission (Figure 3). These discrepancies highlight the value of the NEWS-2 score in guiding hospital admission decisions for patients with COVID-19 pneumonia, aligning with recommendations from various clinical practice guidelines [13].

Discussion

Given the absence of a specific treatment for SARS-CoV-2, therapeutic interventions primarily focus on mitigating the inflammatory response, particularly addressing ARDS and the cytokine storm, which are critical factors in the severity of the disease [8,14]. The impact of delayed ICU admission on clinical outcomes and hospital stay remains unclear [5]. This study provides novel insights, revealing that mortality rates among patients with COVID-19 pneumonia requiring

Figure 2. Survival functions by robust Cox model, according to ICU admission type: EICUA vs LICUA.

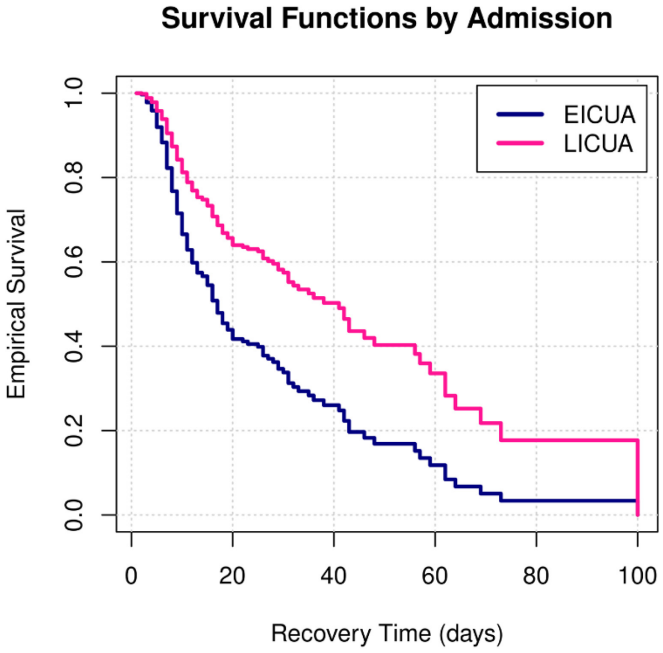


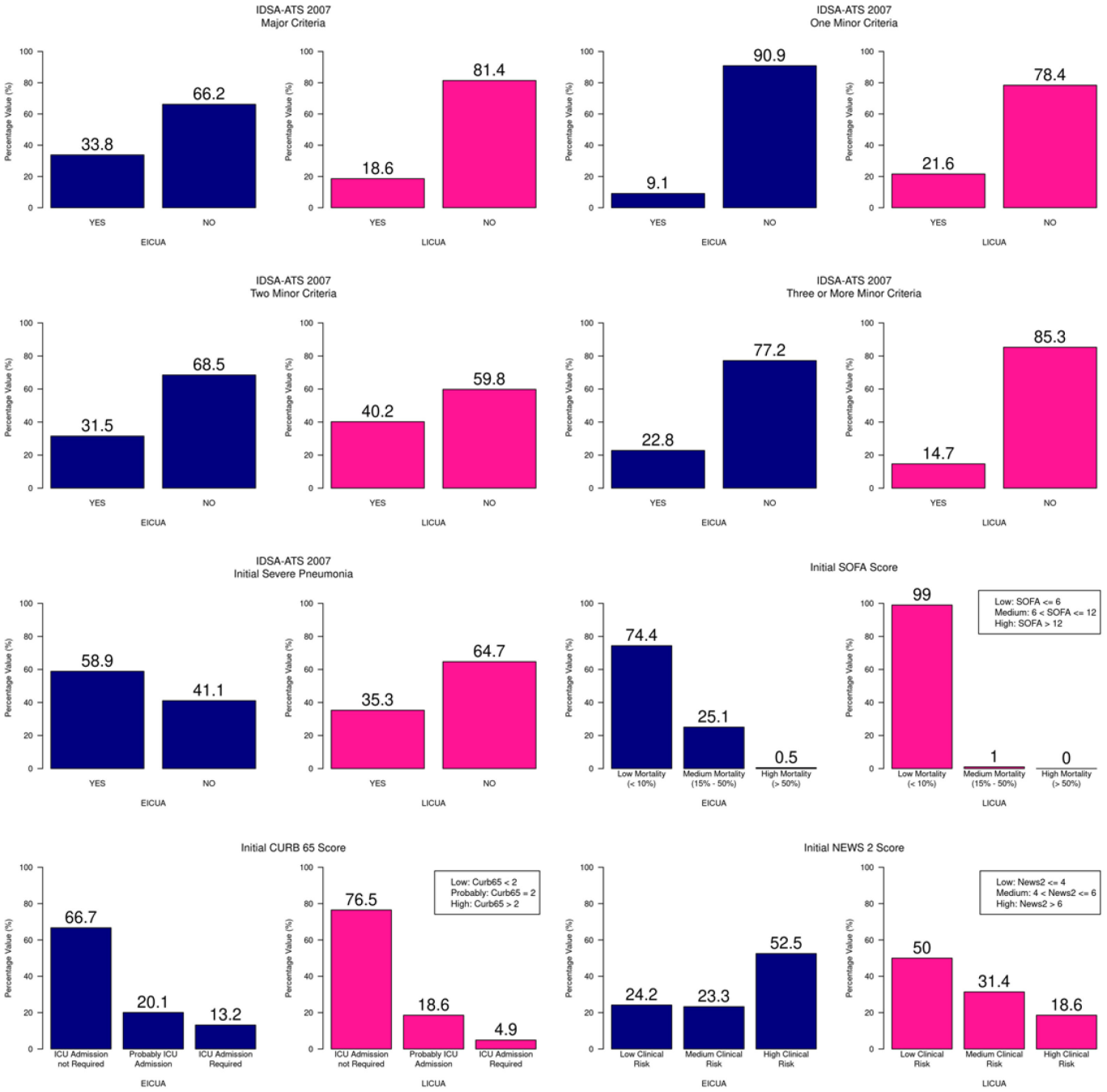
Table 4. Logistic regression for status of patients after ICU care.

MODEL 1: Logistic Model (McFadden pseudo-R squared index = 0.016)			
Variable	**Coef.**	**S.E.(Coef)**	***p***
Intercept	-0.637	0.283	0.025
Admission-type (0 – EICUA and 1 – LICUA)	0.456	0.285	0.109
Colchicine (0 – Yes and 1 – No)	0.589	0.328	0.072
Corticosteroids (0 – Yes and 1 – No)	-0.263	0.301	0.383
Comorbidities (0 – Yes and 1 – No)	-0.363	0.266	0.171
Sex (0 – Male and 1 – Female)	-0.16	0.247	0.517
MODEL 2: Stepwise-Logistic Model (McFadden pseudo-R squared index = 0.009)			
Variable	**Coef.**	**S.E.(Coef)**	***p***
Intercept	-0.812	0.262	0.002
Admission-type (0 – EICUA and 1 – LICUA)	0.492	0.28	0.079
Colchicine (0 – Yes and 1 – No)	0.403	0.275	0.142

ICU admission—whether early from the emergency department or late from the hospitalization service—did not significantly differ. Similarly, ICU stay and mechanical ventilation duration did not show significant differences between the two groups. However, EICUA patients exhibited statistically significant reductions in both recovery time, measured as time to ICU discharge, and hospital stay. To our knowledge, this is the first study to assess these differences in COVID-19 pneumonia.

In the context of community-acquired pneumonia (CAP), few epidemiological studies have investigated the timing of admission and its correlation with clinical outcomes. Restrepo *et al.* [4] reported higher 30-day mortality in a retrospective cohort of 161 CAP patients admitted late to the ICU compared to those admitted early (47.4% vs. 23.2%, $p = 0.02$; HR = 2.6, 95% CI: 1.2-5.5, $p = 0.02$), though this study had a small LICUA population (19 patients vs. 142 in EICUA). In a broader study of CAP patients over 64 years old, ICU admission

Figure 3. Prevalence of Pneumonia by ICU type according to different scores.



was associated with lower 30-day mortality compared to general ward admission (14.8% vs. 20.5%, $p = 0.02$) [5], but the timing of ICU entry was not evaluated.

Conversely, a study at the Veterans Affairs Hospital noted extended hospital stays (12 vs. 7 days, $p = 0.07$) and higher 30-day mortality (23% vs. 4%, $p < 0.01$) in ICU-admitted CAP patients, without specifying admission timing [1]. In our study, therapy primarily included high-dose corticosteroids (methylprednisolone) before ICU admission, later adjusted to dexamethasone 6 mg/day during ICU care (85.9% vs. 64.2%). Although mortality was lower, this difference was not statistically significant. Other studies have shown the positive impact of corticosteroids at various doses on mortality and the need for ICU admission [8,15,16]. Pinzón *et al.* found that high-dose methylprednisolone significantly reduced severity markers and mortality in COVID-19 pneumonia compared to dexamethasone, with notable decreases in CRP, D-Dimer, and LDH levels, and reduced ICU transfers (4.8% vs. 14.4%) and mortality (9.5% vs. 17.1%), alongside a shorter recovery time (3 vs. 6 days, $p < 0.0001$) [17,18].

In a cohort study of 201 COVID-19 pneumonia patients, those with ARDS who received methylprednisolone had a lower mortality rate (46% vs. 61.8% for those who did not receive it; HR = 0.38, 95% CI: 0.20-0.72, $p = 0.003$). However, these results should be interpreted with caution due to the small sample size [8]. Ko *et al.*, in a retrospective cohort study, compared 104 patients receiving methylprednisolone at 1 mg/kg/day for three or more days with 83 patients receiving dexamethasone at 6 mg/day for seven or more days. The mortality rate for those requiring mechanical ventilation was 42% lower in the high-dose group (16.4% vs. 26.5%; HR = 0.48, 95% CI: 0.24-0.96, $p = 0.0385$). Further randomized studies are needed to clarify the effects of these doses [15].

The overall mortality in our study was 40.5%, in contrast to the RECOVERY trial, where 28-day mortality was 22.9% [19,20]. Although the reasons for this discrepancy are unclear, our study documented statistically significant differences in laboratory variables between EICUA and LICUA patients, unlike the RECOVERY trial, which did not report on mortality-related laboratory variables such as LDH, D-Dimer, and CRP [8]. Studies on corticosteroid administration in COVID-19 pneumonia have demonstrated improved outcomes with early administration. Monedero *et al.* found that early administration of corticosteroids within the first 48 hours was associated with a mortality rate of 30.3%, compared to 44.2% with delayed administration [21]. Notably, 42% of EICUA patients in our study had mild to moderate ARDS without established respiratory failure, highlighting significant public health implications given the limited availability of ICU beds during the pandemic.

Limitations of this study include its retrospective design, the relatively small population size compared to the total number of ICU admissions, and the potential influence of other unexamined factors on patient outcomes. Bed availability may have affected results, although patients requiring ICU admission were promptly transferred elsewhere if beds were unavailable. Despite these limitations, this study offers valuable insights as the first to compare outcomes based on ICU admission timing in COVID-19 pneumonia, with a 30-day follow-up facilitating comparison with existing literature.

Conclusions

The mortality of patients with COVID-19 pneumonia requiring admission to the ICU, whether early or late, did not show statistically significant differences between the two groups. However, our findings reveal notable differences in recovery time, the likelihood of immediate recovery or ICU discharge, and the duration of hospital stay, with EICUA patients showing more favorable outcomes compared to LICUA patients. These results suggest that implementing a well-structured institutional protocol, such as that proposed by Pinzón *et al.* [17], along with thorough medical evaluation during hospitalization, can positively influence patient outcomes. To validate these findings further, randomized controlled trials are needed.

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Authors' Contribution

Conceptualization: M.A.P., N.F., J.F.B., H.H., P.M., B.J.M., B.R., C.A.A., I.P., L.M.T., J.Q. Data Curation: S.O. Formal Analysis: M.A.P., S.O., H.L., N.F., H.H., B.J.M., B.R., I.P., J.Q. Investigation: M.A.P., S.O., H.L., J.F.B., H.H., P.M., C.A.A., L.M.T. Methodology: M.A.P., S.O., H.L., N.F., J.F.B., H.H., P.M., B.J.M., B.R., I.P., J.Q. Project

Administration: M.A.P., S.O. Software: S.O. Supervision: M.A.P., S.O., H.L., N.F., J.F.B., H.H., B.R., C.A.A., L.M.T. Validation: M.A.P., S.O., H.H., N.F. Writing-original Draft: M.A.P., S.O., H.L., H.H. Writing-review & Editing: M.A.P., S.O., H.L.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Ethical Considerations

This study was conducted according to the guidelines of the Helsinki Declaration of the World Medical Association. Moreover, it is based on resolution 8430 of 1993 (Ministry of Health of Colombia), which establishes the scientific, technical, and administrative standards for health research. According to Chapter I, Article 11 of this resolution, the study was classified as risk-free research. Finally, this research had the approval of both the Ethical and Research Committees of CMGQ and NCSC (Act 01-2021 and EM 2021002).

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