Association between lung involvement, risk factors and outcomes in COVID-19 patients treated at a reference hospital in Paraíba

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ABSTRACT

Objective: To assess the association between the degree of lung involvement (LI) on chest CT scans of COVID-19 patients, risk factors and outcomes. **Methods:** Observational and retrospective study of 284 COVID-19 patients. Age, sex, clinical presentation, oxygen saturation on admission, risk factors, time after symptom onset, percentage of LI, length of stay in ward and ICU, duration of ETI, and death were assessed. 3 groups were created according to the LI. **Results:** 167 patients had an involvement of <25%; 80, 25-50%; and 37, >50%. The group with greater LI was older, had more males and a higher incidence of cough, dyspnea and some comorbidity. Moreover, the group with greater LI had lower saturation on admission, more ETI, more admissions to the ward or ICU, and higher mortality. LI, ETI and age were predictors of mortality. **Conclusion:** The degree of LI appears to be significantly associated with some clinical parameters, need for hospitalization, intubation, and death.

Keywords: COVID-19, Risk factors, Multidetector computed tomography.

INTRODUCTION

In December 2019, an outbreak of pneumonia of unknown origin began in Wuhan, China. Named by the World Health Organization (WHO) as *"coronavirus disease 2019"* (COVID-19) and caused by the novel coronavirus, SARS-CoV-2, the disease spread rapidly around the world growing to pandemic proportions[1].

The spectrum of clinical presentations is broad, with most lung infections being mild. Severe and critical forms are reported especially in the elderly and people with comorbidities. The most frequent tomographic findings are ground-glass opacities, consolidations having a predominantly peripheral distribution, crazy-paving pattern, vascular thickening, and reversed halo sign[2].

Reverse-transcription polymerase chain reaction (RT-PCR) is considered the reference standard for the diagnosis of COVID-19 infection, but chest computed tomography (CT) has a higher sensitivity for early detection of the disease, especially in patients with high clinical suspicion and an initial negative RT-PCR test[3], and may also indicate the disease's stage[4] and adverse outcomes[5]. For example, studies report that greater lung involvement in chest CT is associated with a higher need for hospitalization and ICU[6].

Among the comorbidities presented by COVID-19 patients, the most frequent is systemic arterial hypertension, followed by diabetes and underlying cardiovascular diseases, which increase the risk of hospitalization and death[7]. In addition, it is pointed out that age > 60 years and male sex are related to a greater progression to severe COVID-19 pneumonia[8].

Few Brazilian studies assess the association between different degrees of lung involvement and clinical parameters and outcomes in COVID-19 patients, which is of significant importance for a greater understanding of the disease, its clinical-tomographic association, as well as its impacts on prognosis.

Therefore, given the relevance of the subject and the important addition of data on COVID-19 for the national scene, the objective of this study

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is to evaluate the association between the degree of lung involvement in chest CT scan of patients infected by SARS-CoV-2 and the risk factors related to this disease, as well as the outcomes. It also aims to analyze a Brazilian experience in dealing with COVID-19, considering the specific characteristics of each service.

METHODS

This is a descriptive, observational and retrospective study, conducted with a random sample of 284 patients who sought emergency care at the Alberto Urquiza Wanderley Hospital – Unimed, a reference for COVID-19 patients in the state and located in the city of João Pessoa, Paraíba, Brazil.

The research took place between May and July 2020, and involved individuals referred to the Diagnostic Imaging Centre (DIC) of the same hospital and performed a chest CT scan. Subsequently, confirmation of the diagnosis was obtained using the RT-PCR method.

The inclusion criteria were cases of patients older than 18 years, who had clinical signs and symptoms suggesting COVID-19 and performed chest CT on admission to the emergency room. For those who underwent more than one CT scan on different admissions, for COVID-19 lung assessment, the result of the last CT performed was considered, as it more reliably represented the evolution of the pulmonary condition associated with the outcome.

Patients with incomplete medical records, as well as those whose CT report did not describe the percentage of pulmonary involvement, were excluded. Participant data were obtained from electronic medical records.

Data collection was based on predefined variables: age, sex, clinical presentation, oxygen saturation in room air on admission, risk factors (age > 60 years, BMI > 30kg/m² and comorbidities), the time between symptoms onset and CT performance (less than or equal to 1 week; more than 1 week), percentage of lung involvement, length of stay, in days, in ward and ICU, in addition to the duration of endotracheal intubation (ETI).

To perform the CT, a Multislice CT scanner was used, through volumetric data acquisition with 1.0mm of collimation, with three-dimensional, multiplanar and volumetric reconstruction techniques. During lung inspiration maneuvers, thin sections of the lung parenchyma were obtained using high-resolution technique without intravenous administration of non-ionic iodinated contrast.

The images were always reported by the same team of radiologists, and the involvement of the parenchyma was manually assessed suing a quantitative method, based on expert consensus.

For comparative analysis, patients were divided into three groups regarding pulmonary involvement: <25% (group 1); 25-50% (group 2); >50% (group 3). The outcomes assessed were hospitalization in the ward or ICU, need for ETI, and mortality.

Results were presented as mean and standard deviation (SD), median, and interquartile ranges or proportions, as appropriate. Regarding continuous variables, groups 1, 2 and 3 were compared using the ANOVA or Kruskal-Wallis test, depending on whether the variables had a normal distribution or not (Shapiro-Wilk test). The Bonferroni test was used to assess which groups had significant differences between them. Furthermore, regarding categorical variables, the different groups (degree of involvement, need for hospitalization in the ward or ICU, need for ETI and mortality) were compared using the $\chi 2$ test or Fisher's exact test, when appropriate.

To assess factors independently associated with the outcome mortality, multivariate logistic regression was performed, which variables with $p<0.05$ in the univariate analysis were included. In this study, values of $p<0.05$ were considered statistically significant and a confidence interval (CI) of 95%. Statistical analyses were performed using the statistical software SPSS, version 23.

The study was approved by the Research Ethics Committee of the Medical Sciences Center of the Federal University of Paraíba (CCM/UFPB), number 4.253.601, CAAE: 36515420.6.0000.8069. The informed consent form (ICF) was waived due to the retrospective nature of the study.

RESULTS

The study involved 284 patients. The mean age was 54,8 years old (SD = 17.2, ranging from 17 to 100 years old) and 151 were women (53.2%). Group 1 included 167 patients (58.8%); group 2, 80 (28.2%); and group 3 included 37 individuals (13%).

As shown in Table 1, the main symptoms reported, during CT performance, were dyspnea (74.1%), cough (72.9%) and fever (64.8%). 50.7% had a time after symptoms onset less than or equal to 1 week. In addition, saturation at the time of admission ranged from 72% to 100%, with a median of 98%.

The most frequent risk factors in the patients included were age > 60 years (35.3%) and the presence of comorbidities (72.2%), in which the most frequent were hypertension (44%), obesity (32.4%) and diabetes (21.8%).

Table 1

Baseline and clinical characteristics of patients according to the degree of lung involvement, Paraíba, Brazil, 2020.

Variable	Degree of lung involvement			p
	<25% N=167	25-50% N=80	>50% N=37	
Demographic profile				
Male sex, n (%)	60/167 (35.9%)	48/80 (60%)	25/37 (67,.6%)	<0.00[1]*
Age [a]	52 [38-61]	55 [43-70]	63 [50-77]	0.001[†]
Time after symptoms onset				
≤ 1 week	89 (53.9)	39 (50)	16 (44.4)	0.408*
> 1 week	76 (46.1)	39 (50)	20 (55.6)	
Clinical presentation				
Oxygen saturation on admission [a]	98.5% [97-99]	96% [94-98]	91% [85-96]	<0.001*
Fever, n (%)	101 (60.5)	57 (71.3)	26 (70.3)	0.202*
Cough, n (%)	113 (67.7)	61 (76.3)	33 (89.2)	0.018*
Sore throat, n (%)	69 (41.3)	30 (37.5)	11 (29.7)	0.430*
Dyspnea, n (%)	96 (57.5)	58 (72.5)	28 (75.7)	0.022*
Headache, n (%)	94 (56.3)	38 (47.5)	13 (35.1)	0.052*
Myalgia, n (%)	108 (64.7)	45 (56.3)	23 (62.2)	0.434*
Chills, n (%)	42 (25.1)	21 (26.3)	3 (8.1)	0.051*
Anosmia/ ageusia, n (%)	53 (31.7)	26 (32.5)	9 (24.3)	0.678*
Expectoration, n (%)	1 (0.6)	0 (0)	0 (0)	1.000*
BMI [a]				
	27 [25-31.5]	29 [26.5-32.9]	29.5 [26-31.8]	0.024[†]

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Table 1

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Variable	Degree of lung involvement			p
	<25% N=167	25-50% N=80	>50% N=37	
Comorbidities				
Presence of comorbidity, n (%)	105 (62.9)	67 (84)	33 (89)	<0.001*
Obesity, n (%)	48 (28.7)	31 (38.8)	13 (35.1)	0.259*
Diabetes, n (%)	27 (16.2)	21 (26.3)	14 (37.8)	0.009*
Hypertension, n (%)	63 (37.7)	41 (51.3)	21 (56.8)	0.034*
Coronary artery disease, n (%)	0 (0)	0 (0)	1 (2.7)	0.130*
Immunodepression, n (%)	7 (4.2)	3 (3.8)	1 (2.7)	1.000*
Cancer, n (%)	0 (0)	1 (1.3)	1 (2.7)	0.090*
COPD, n (%)	1 (0.6)	0 (0)	1 (2.7)	0.323*
Chronic lung disease, n (%)	14 (8.4)	5 (6.3)	4 (10.8)	0.636*
Cardiovascular disease, n (%)	9 (5.4)	7 (8.7)	7 (18.9)	0.028*
Kidney disease, n (%)	3 (1.8)	5 (6.2)	1 (2.7)	0.158*
Neurological diseases, n (%)	1 (0.6)	7 (8.8)	2 (5.4)	0.002*

[a] Values expressed as median [interquartile range]; *Fisher' exact test; †Kruskal-Wallis test.

BMI: body mass index. COPD: Chronic Obstructive Pulmonary Disease.

It was found that, in general, required hospitalization in the ward or ICU, varying according to the degree of lung involvement (Table 2). In the multivariate analysis, greater lung involvement was a predictor of mortality.

Table 2

Association between the degree of lung involvement and clinical outcomes, Paraíba, Brazil, 2020.

Variable	Degree of lung involvement			p
	<25% N=167	25-50% N=80	>50% N=37	
Outcomes				
Need for hospitalization in ward or ICU, n (%)	18 (10.8)	53 (66.3)	34 (94.4)	<0.001*
Place of hospitalization, n (%)				
Ward	18 (10.8)	51 (63.8)	31 (86)	<0.001*
ICU	5 (3)	19 (23.8)	12 (32.4)	<0.001*
Length of stay in [a]				
Ward	6 [6-11.5]	7 [5-11]	9 [5-11.5]	0.955†
ICU	22 [4-13]	13 [2.5-13]	9 [4-10]	0.525†
Need for endotracheal intubation, n (%)	2 (1.2)	10 (12.5)	8 (21.6)	<0.001*
Length of intubation [a]	9.5 [8.8-10.3]	12 [5.3-15.8]	10 [6.3-17.3]	0.941†
Mortality, n (%)				
Hospital discharge, n (%)	164 (98.2)	70 (89.7)	25 (73.5)	<0.001*
Death, n (%)	3 (1.8)	8 (10.3)	9 (26.5)	

[a] Values expressed as median [interquartile range]; * Fisher' exact test; †Kruskal-Wallis test.

ICU: intensive care unit.

Table 3 shows demographic and clinical aspects according to the need for hospitalization (in ward or ICU), need for endotracheal intubation and mortality.

Among those admitted to the ICU, 20 patients (55.5%) required ETI (median time = 9.5 days). In addition, 20 patients (7%) died due to COVID-19 complications.

Of the 33 patients who needed hospitalization in ICU, 19 (57.6%) died. The median time from ICU admission to death was 10 days, ranging from 1 to 31 days, while, for ward and ICU, it was 19 days, ranging from 19 to 144 days.

The mean total hospital stay was 25 days for those who died, and 10.3 days for those who survived. For patients admitted to the ICU and were discharged the median time in the ICU was 3.5 days. For admitted to the ward and ICU, the median time was 9 days, ranging from 1 to 79. Finally, of the 20 patients who required ETI, 80% died.

Table 3

Baseline and clinical characteristics of patients according to the outcomes for the 284 patients evaluated, Paraíba, Brazil, 2020.

Variables	Need for hospitalization			Need for intubation			Mortality		
	Yes N=105	No N=179	p	Yes N=20	No N=264	p	Death N=20	Hospital Discharge N=264	p
Demographic profile									
Male sex, n(%)	63(60)	69(39)	0.001*	8(40)	125(47.3)	0.687*	10(50)	120(46.3)	0.939*
Age[a]	62.5 [49-76]	50 [38-60]	<0.001†	73 [61-81]	53 [40-66.5]	<0.001†	79 [73-82.5]	53 [39-64]	<0.001†
Time after symptoms onset									
≤1 week	56(53.3)	87(49.2)	0.729*	12(60)	132(50)	0.074*	13(68)	129(50.6)	0.022*
>1 week	47(44.8)	87(49.2)		7(35)	128(48.5)		6(30)	126(49.4)	
Clinical presentation									
Oxygen saturation on admission [a]	95% [90.3-97]	98% [97-99]	<0.001†	89% [86.5-93.5]	98% [96-99]	<0.001†	88,5% [82.5-94.5]	98% [96-99]	<0.001†
Fever, n(%)	75(71.4)	108(61)	0.101*	13(65)	171(64.8)	1.000*	12(60)	167(64.5)	0.872*
Cough, n(%)	88(83.8)	118(66.7)	0.002*	15(75)	192(72.7)	1.000*	13(65)	189(73)	0.611*
Sore throat, n(%)	33(31.4)	77(43.5)	0,059*	5(25)	105(39.8)	0.284*	5(25)	104(40.2)	0.236††
Dyspnea, n(%)	79(75.2)	101(57.1)	0.003*	17(85)	165(62.5)	0.053†	17(85)	161(62.2)	0.052††
Headache, n(%)	44(41.9)	101(57.1)	0.019*	8(40)	137(51.9)	0.427*	6(30)	137(52.9)	0.082*
Myalgia, n(%)	59(56.2)	117(66.1)	0.125*	10(50)	166(62.9)	0.365*	8(40)	167(64.5)	0.052*
Chills, n(%)	20(19)	46(26)	0.235*	3(15)	63(23.9)	0.582††	2(10)	63(24.3)	0.178††
Anosmia/ ageusia, n(%)	25(23.8)	63(35.6)	0.053*	4(20)	84(31.8)	0.325††	2(10)	86(33.2)	0.043††
Expectoration, n(%)	0(0)	1(0.6)	1.000††	0(0)	1(0.4)	1.000††	0(0)	1(0.4)	1.000††
BMI[a]	29 [26.2-32.7]	28 [25.2-31.7]	0.054†	29 [25.3-31.6]	28 [25.6-32.2]	0.998†	26 [25-30]	28 [25.7-32.4]	0.158†

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Table 3

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Variables	Need for hospitalization			Need for intubation			Mortality		
	Yes N=105	No N=179	p	Yes N=20	No N=264	p	Death N=20	Hospital Discharge N=264	p
Comorbidities									
Presence of comorbidity, n(%)	88(83.8)	116(65.5)	0.001*	18(90)	187(70.8)	0.073*	18 (90)	183(70.7)	0.072*
Obesity, n(%)	38(36.2)	54(30.5)	0.380*	6(30)	91(34.5)	0.871*	4(20)	88(34)	0.222*
Diabetes, n(%)	33(31.4)	29(16.4)	<0.001*	7(35)	55(20.8)	0.288*	9(45)	52(20.1)	0.031*
Hypertension, n(%)	60(57.1)	64(36.2)	0.001*	10(50)	115(43.6)	0.744*	11(55)	111(42.9)	0.412*
Coronary artery disease, n(%)	1(1)	0(0)	0.372††	0(0)	1(0.4)	1.000††	0(0)	1(0.4)	1.000††
Immunodepression, n(%)	4(3.8)	7(4)	1.000††	0(0)	11(4.2)	1.000††	0(0)	9(3.5)	1.000††
Cancer, n(%)	2(1.9)	0(0)	0.138††	1(5)	1(0.4)	0.136††	1(5)	0(0)	0.072††
COPD, n(%)	2(1.9)	0(0)	0.138††	1(5)	1(0.4)	0.136††	1(5)	1(0.4)	0.138††
Chronic lung disease, n(%)	7(6.7)	16(9)	1.000*	3(15)	20(7.6)	0.085††	3(15)	20(7.7)	0.091*
Cardiovascular disease, n(%)	15(14.3)	8(4.5)	0.007*	3(15)	20(7.6)	0.213††	6(30)	16(6.2)	<0.001††
Kidney disease, n(%)	5(4.8)	4(2.3)	0.3††	1(5)	8(3)	0.487††	1(5)	8(3.1)	0.493††
Neurological diseases, n(%)	9(8.6)	1(0.6)	0.001††	3(15)	7(2.7)	0.043††	5(25)	4(1.5)	<0.001††

[a] Vales expressed as median [interquartile range]; *Chi-squared test; †Mann-Whitney test; †† Fisher's exact test.

BMI: body mass index; COPD: chronic obstructive pulmonary disease.

DISCUSSION

Similar to the findings in our study, authors have demonstrated that an increasing extent of lung parenchyma involvement on chest CT independently predicts the risk of clinical deterioration or death, with an additional prognostic value regarding isolated clinical parameters.[9] They also add that it is significantly associated with the need for mechanical ventilation,[10-11] the stage of disease progression,[10] and early death or ICU admission in hospitalized patients, especially in those with lung involvement > 50%.[12]

In our sample, men had greater lung involvement and need for hospitalization. Similarly, the literature shows that the male sex has a strong positive correlation with the increase in the CT severity score[13] and women have a lower risk of ICU admission.[14-16] However, we did not observe a significant association between male sex and increased mortality, as reported in a study in Rio de Janeiro,[17] despite discordant observations in a Danish cohort[14] and a study conducted in the city of São Paulo.[18]

As evidenced by our research, other studies indicate a significant correlation between age and the severity of lung involvement,[13] which is also referred to as a risk factor for severe COVID-19 pneumonia and ICU admission.[15]

Although we observed a significant association between age and the need for ETI, this data is conflicting in the literature. While some authors reported results similar to ours,[19] others did not observe a statistically significant association.[20] At the national level, in the bivariate analysis presented by a study conducted in a private hospital in Porto Alegre, age > 65 years was more likely to require IMV.[11]

Age was also associated with death, also being, in the multivariate analysis, an independent predictor of mortality, corroborating with other publications that associate this variable with a higher risk of death.[16-18,21-22]

Regarding the time between symptoms onset and CT performance, our study did not observe a significant difference between the different degrees of lung involvement, probably because this data is related to time taken to seek medical care and perform the CT, as well as because the degree of lung involvement was much more associated with the patient's profile than with time after symptoms onset.

For Ruch et al. (2020), the time taken to perform the CT was shorter among patients with lung involvement < 25%, with a difference of only 1 day, so the authors themselves questioned the clinical relevance of this finding.[12]

However, we found a significant difference between the time after symptoms onset and CT performance and mortality, which was not seen in regard to the need for hospitalization or intubation. Notwithstanding, this difference was not observed in other studies,[22-23] which compared the duration of symptoms at admission between the group of survivors and those who died.

In our sample, oxygen saturation in room air on admission differs from other authors,[24] according to whom it was generally low, with a median of 87% and a range from 77 to 92%. In addition, lower saturation on admission was significantly associated with a greater degree of lung involvement, need for hospitalization, intubation and death, which was also reported in the literature.[24-25]

Regarding the clinical presentation, the main symptoms reported were dyspnea, cough and fever, as also described by Hur et al. (2020) and Vahey et al (2021).[26-27] However, in our study, an important difference was found only in the prevalence of cough and dyspnea between the groups of lung involvement and the need for hospitalization, probably due to the intrinsic relationship between those symptoms and the involvement of the lower airways. However, headache was more frequently reported, with a significant difference in the group that did not require hospitalization. In this context, Vahey at al. (2021) demonstrated that the presence of dyspnea was associated with a higher chance of hospitalization, but, on the other hand, headache, dry cough, ageusia and anosmia were associated with a lower risk of hospitalization.[27] Similarly, among the COVID-19 cases registered in Acre between March 15, 2019, and September 1st, 2020, headache was among the signs and symptoms related to a better prognosis.[28]

Moreover, no symptom was significantly associated with the need for intubation, but, in terms of mortality, it was found that myalgia and anosmia/ageusia were less frequent in the death group. A systematic review[29] showed that fever, cough, sore throat, dyspnea, headache and expectoration were not significantly associated with mortality.

According to our research, comorbidities were significantly associated with the degree of lung involvement and the need for hospitalization in the ward or ICU. In the literature, patients with underlying conditions were the majority when lung involvement was > 50%.[10] However, other authors do not report a relevant association between the presence of comorbidities (diabetes, hypertension, heart failure, chronic pulmonary disease, immunodepression, active malignancy) and the extent of CT involvement.[12]

Moreover, studies have demonstrated that patients who presented clinical deterioration (ICU admission, invasive mechanical ventilation, or vasopressor therapy) or death had more underlying conditions, such as diabetes, hypertension, hyperlipidemia, cardiovascular, oncological, and chronic kidney diseases, and immunodeficiency.[5,9]

Regarding the need for ETI, Hur et al. (2020) showed that the only important difference between intubated and non-intubated patients was the higher presence of diabetes among those who needed intubation.[26] On the other hand, in our sample, only neurological diseases were associated with this outcome.

In general, there is strong evidence in the scientific community that the absence of comorbidities is higher among individuals who survive COVID-19,[23] while the presence is significantly higher among patients who die,[21] thus our study obtained results agreeing with this aspect.

We also observed that the mean length of hospital stay among the patients who died was longer than that found by other authors,[30] what may be related to the fact that, in our sample, a smaller number of deaths was evaluated, as well as there was a large discrepancy regarding

one of the patients' length of hospitalization, which was 144 days, increasing the mean value.

On the other hand, the average length of stay in the ICU was similar to that found by Grasselli et al. (2021) and Yang et al. (2020),[31-32] what may be related to similar indications for ICU admission, with no influence from the characterization of the sample selected for the study, as well as the progression of the disease in individuals most severely affected. Similarly, the mortality rate among patients who required ETI was similar to the literature.[33]

The study had limitations related to its retrospective design, such as the incomplete or missing data in medical records, which, however, was compensated by the appropriate sample size. Limited data were mainly related to smoking and smoking load; thus, it was not possible to make any association between this habit and other variables involved in the study. Another limitation was the scarcity of national studies that addressed the outcomes associated with the degree of lung involvement due to COVID-19, which impaired the comparison between our findings and other Brazilian scenarios. Nevertheless, these aspects did not affect the development of this research, which highlights this analysis in the national scene.

CONCLUSION

Our research showed that there was a positive correlation between the degree of lung involvement and the outcomes (hospitalization, intubation, and death), reinforcing the importance of the chest computed tomography in COVID-19 patients as a predictor of prognosis, which is fundamental for a better clinical follow-up and shows the need for other Brazilian studies to also contribute to this observation.

Therefore, it is highlighted the importance of early recognition of clinical and tomographic signs suggestive of severity in COVID-19 patients, in order to identify possible complications of the disease and, thus, promote optimal treatment. In addition, the information brought by this study can be compared with data from other studies, in a brief future, for a better characterization of the pandemic in the country, as well as the mortality related to it.

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RMMF, WAC, AAC, AASF, BFS, ACF, BPS, RPBC: design and delineation of the study; analysis and interpretation of the data; writing and critical review relevant to the intellectual content of the manuscript; final approval of the version to be published; responsibility for all aspects of the work, including ensuring its accuracy and integrity.

JFP: design and delineation of the study; analysis and interpretation of the data; critical review relevant to the intellectual content of the manuscript; final approval of the version to be published; responsibility for all aspects of the work, including ensuring its accuracy and integrity.

PAS: design and delineation of the study; critical review relevant to the intellectual content of the manuscript; final approval of the version to be published; responsibility for all aspects of the work, including ensuring its accuracy and integrity.

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