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LETTER TO THE EDITOR

WILEY

Obese COVID-19 patients show more severe pneumonia lesions on CT chest imaging

The COVID-19 epidemic will persist for the foreseeable future. Given the significant toll the outbreak has taken on the healthcare system, identifying those patients with a greater need for medical attention is necessary. Recent studies suggest that obesity is associated with worse severity of COVID-19 pneumonia, increasing the need for hospitalization, critical care and mechanical ventilation.[1–6]

TABLE 1 Demographics, medical history, laboratory and pneumonia involvement (mm^3) for the four BMI groups

Variables	Normal weight (n = 84, 36.4%)	Overweight (n = 105, 45.4%)	Obese (n = 33, 14.3%)	Underweight (n = 9, <0.1%)	F/χ^2 value	*P*
Age, years	43.1 ± 14.2	47.7 ± 12.0	44.8 ± 13.3	49.1 ± 13.7	2.2	.1
Female/male patients (%)	39/45 (46.4)	43/62 (41.0)	9/24 (27.3)	3/6 (33.3)	3.8	.3
Onset to hospitalization, days	6.8 ± 6.2	7.0 ± 6.4	6.0 ± 6.1	6.9 ± 5.7	0.2	.9
Diabetes, yes/no (%)	5/79 (6.0)	6/99 (5.7)	1/32 (3.0)	1/8 (11.1)	0.9	.6
Hypertension, yes/no (%)	8/76 (9.5)	15/90 (14.3)	4/29 (12.1)	0/9 (0)	2.3	.7
Cardiovascular disease, yes/no (%)	1/83 (1.2)	3/102 (2.9)	0/33 (0)	0/9 (0)	1.7	.5
Hyperlipidaemia, yes/no (%)	0/84 (0)	1/104 (1.0)	2/31 (6.1)	0/9 (0)	7.2	.1
Liver disease, yes/no (%)	3/81 (3.6)	2/103 (1.9)	0/33 (0)	0/9 (0)	1.7	.2
Cancer, yes/no (%)	1/83 (1.2)	1/104 (1.0)	0/33 (0)	0/9 (0)	0.5	.5
Lung-related disease, yes/no (%)	2/82 (2.4)	1/104 (1.0)	1/32 (3.0)	0/9 (0)	1.1	.5
C-reactive protein, mg/L	13.1 ± 22.4	20.5 ± 23.8	30.1 ± 29.0	18.7 ± 22.7	4.1	**.01***
Whole lung, mm^3						
Total lesion	99.4 ± 142.9	193.9 ± 267.9	251.3 ± 348.6	191.7 ± 220.3	3.9	**.01***
Whole GGO	76.7 ± 117.0	146.1 ± 205.1	192.1 ± 259.2	173.5 ± 210.3	3.9	**.01***
Whole consolidation	22.6 ± 37.1	47.8 ± 76.8	59.2 ± 111.1	18.2 ± 20.4	3.2	**.02***
Right superior lobe, mm^3						
Total lesion	8.6 ± 29.2	32.2 ± 81.2	48.0 ± 86.2	19.6 ± 34.8	3.4	**.02***
GGO	7.5 ± 26.6	25.8 ± 65.5	36.6 ± 63.4	18.7 ± 33.1	3.0	**.03***
Consolidation	1.1 ± 3.8	6.3 ± 20.5	11.4 ± 27.7	0.9 ± 1.8	3.2	**.02***
Right middle lobe, mm^3						**.03**
Total lesion	3.0 ± 10.6	7.4 ± 19.7	11.9 ± 21.3	1.8 ± 2.4	2.7	**.05**
GGO	2.6 ± 9.2	6.4 ± 17.3	10.0 ± 17.4	1.7 ± 2.3	2.5	.06
Consolidation	0.3 ± 1.7	1.0 ± 3.1	1.9 ± 4.9	0.1 ± 0.1	2.4	.07
Right inferior lobe (mm^3)						
Total lesion	42.1 ± 62.0	69.8 ± 94.2	90.8 ± 113.7	85.6 ± 96.6	3.2	**.03***
GGO	31.6 ± 48.0	48.7 ± 65.8	68.5 ± 82.7	72.4 ± 80.3	3.4	**.02***
Consolidation	10.5 ± 20.1	21.1 ± 34.2	22.4 ± 40.4	13.3 ± 19.6	2.3	.08
Left superior lobe, mm^3						
Total lesion	9.5 ± 24.5	27.0 ± 55.0	39.6 ± 72.4	23.6 ± 38.0	3.6	**.01***
GGO	7.9 ± 21.9	22.2 ± 45.8	32.9 ± 60.5	23.1 ± 37.5	3.5	**.02***
Consolidation	1.6 ± 4.3	4.7 ± 12.9	6.7 ± 16.7	0.5 ± 0.5	2.4	.07
Left inferior lobe, mm^3						
Total lesion	36.1 ± 58.0	57.5 ± 86.4	61.0 ± 88.9	61.1 ± 97.4	1.5	.2
GGO	27.1 ± 45.4	42.8 ± 66.9	44.1 ± 61.8	57.5 ± 94.7	1.6	.2
Consolidation	9.0 ± 16.8	14.7 ± 22.6	16.8 ± 33.9	3.5 ± 4.0	1.9	.1

Abbreviations: BMI, body mass index; GGO, ground-glass opacity.

*Represents a significant difference between COVID-19 patients with normal BMI and obese COVID-19 patients ($P < 0.05$, Bonferroni-corrected).

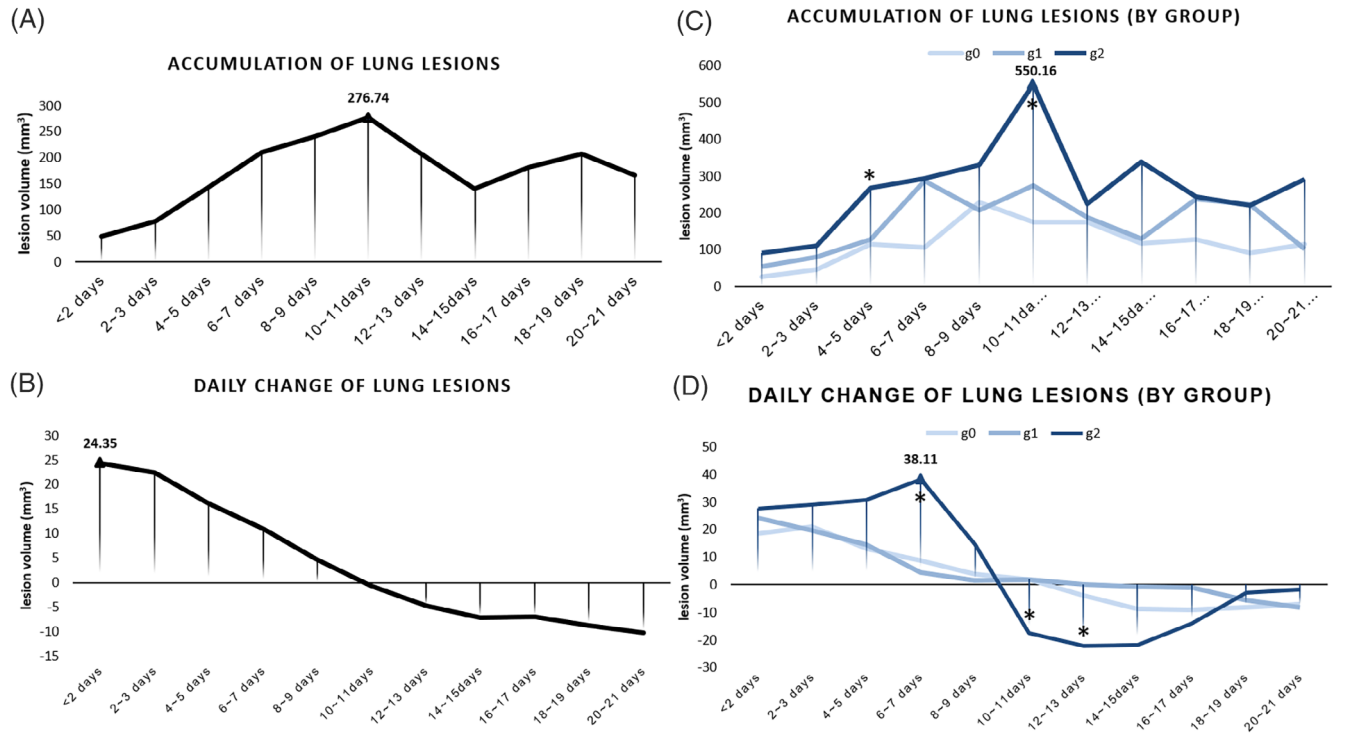

FIGURE 1 Chest computed tomography developmental trajectory in BMI groups. **A**, Across subjects, the total pulmonary lesion volume increased during the 10–11 days after symptom onset (peak: 276.74 mm^3), then gradually decreased. **B,** Positive values for pneumonia lesions change per day were recorded before 10–11 days, then gradually decreased. **C,D**, Obese patients (g2, dark blue) had the greatest pneumonia lesions volume at 10–11 days (peak: 550.16 mm^3), and lesions progressed fast before 7 days (maximum value at 6–7 days, 38.11 mm^3/d). Overweight COVID-19 patients (g1, blue) and those with normal BMI (g0, light blue) had the greatest lesion volume at 6–7 days (peak: 287.6 mm^3) and 8–9 days (peak: 227.86 mm^3), respectively; additionally, overweight COVID-19 patients and those with normal BMI had maximum lesions at days 2–3 . *Represents a significant difference of pulmonary lesion volume among the three groups; then *post hoc t*-tests showed that obese group had greater pneumonia lesions volume, and faster lesion volume growth or absorption than the normal BMI group ($P < 0.05$, Bonferroni-corrected)

However, the trajectory of COVID-19 development is unclear, especially in obese patients. Chest computed tomography (CT) is a valuable method of monitoring COVID-19 severity, and provides an opportunity to explore this question.[7–12] Artificial intelligence (AI) has been successfully applied to chest CT segmentation with high repeatability.[13] In the present study, we used AI-supported CT lesion quantification to evaluate the daily accumulation of lung lesions and aimed to determine the period during which pneumonia developed fastest in obese patients.

We enrolled 231 patients with laboratory-confirmed COVID-19, who were admitted to nine designated hospitals for treatment between January 20 and March 11, 2020 (Appendix S1). Clinical information, chest CT and laboratory data were collected (Appendix S2). As previously, we defined underweight, normal, overweight and obese as a body mass index (BMI) <18.5, 18.5–22.9, 23.0–26.9 and ≥27 kg/m^2, respectively.[14] Based on AI segmentation, we estimated the volume of total pneumonia lesions, ground-glass opacity (GGO) and consolidation, and calculated accumulated pneumonia lesions (mm^3) and volume changes (mm^3/d; Appendix S3).[15,16] We used ANOVA to examine the differences in clinical information, laboratory and pneumonia lesions among groups, followed by *post hoc t*-tests ($P < 0.05$). We then explored the relationships between BMI, pneumonia lesions and laboratory results based on Pearson correlation ($P < 0.05$).

Obese patients had greater total lesion and GGO volume in the whole/bilateral superior/right inferior lung lobe and greater consolidation in the right superior lung than patients with normal BMI ($P < 0.05$; Table 1). Results remained mostly unchanged after correction for lung volume (Appendix S4), personal disease history and demographics (Appendix S5). However, only trends were observed for greater pneumonia lesion volume in overweight and underweight patients compared with those with normal BMI ($P > 0.05$). Additionally, BMI was correlated with total lesions ($r = 0.19$, $P = 0.004$) and consolidation ($r = 0.21$, $P = 0.001$). Regarding laboratory results, obese patients had higher C-reactive protein levels than patients with normal BMI ($P < 0.05$). Across groups, C-reactive protein was related to total lesions, GGO and consolidation ($r = 0.52$, 0.51 and 0.44, respectively; $P < 0.001$). Longitudinally, across groups, total lesion volume increased during the first 10 days after symptom onset (peak: 276.74 mm^3) then gradually decreased; lesions accumulated during the first 10 days, while the progression rate steadily

decreased (Figure 1A,B). In obese patients, lesion volume peaked at 10 days (550.16 mm^3), and there was rapid lesion growth before day 7 (peak: 38.11 mm^3/d). By contrast, overweight patients and those with normal BMI experienced decelerating and slower lesion growth, with the peak lesion and lesion accumulation rate being lower than in obese patients (Figure 1C,D).

Conclusively, obese COVID-19 patients had more diffuse pneumonia lesions than those with normal BMI, with lesions extending from inferior to superior lobes.[17–19] The right inferior lobe was most often involved, which may be attributed to the anatomical features of the right inferior lobar bronchus (straighter and steeper than the others). Regarding pneumonia features, GGO predominates the lesions, suggesting that the pulmonary interstitium is susceptible to COVID-19 virus invasion.[8,17,18,20] Longitudinally, obese patients had a more severe disease course than patients with normal BMI, which is consistent with evidence that these patients had worse disease prognosis.[21] Interestingly, studies have also reported that obesity is associated with worse prognosis in other respiratory viruses (eg, H1N1 influenza).[22–25] We thus inferred that the obesity effects on viral pneumonia were non-specific. Notably, one report contradicted our results and showed that the BMI was not closely associated with the severity of COVID-19.[26] Different ethnic groups and disease stages may account for the discrepancy between the two studies.[27]

The C-reactive protein results of obese patients with COVID-19 partly supported the hypothesis that an aggravated inflammation process is a critical element in disease progression in obese patients.[28–30] Other potential mechanisms include the possibility that COVID-19 virus has a high affinity for human ACE2 (receptors highly expressed in adipose tissue), and obesity-related comorbidities may aggravate pneumonia.[31–35] Additionally, underweight COVID-19 patients had similar lesion volumes to overweight patients. Both underweight and overweight COVID-19 patients had increased trend of lesion volumes than normal BMI patients ($p>0.05$). An adipose tissue imbalance-related immune response in underweight patients may account for these unexpected results. However, the small sample of underweight patients inevitably weakens this finding; further studies are needed. Another limitation of this work is that heterogeneous CT parameters may have had an impact on lesion segmentation.

The Ethics Committee of the Second Affiliated Hospital of the Zhejiang University of Medical School approved our study. All patients provided written informed consent.

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CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

X. L., Y. J. and M. Z. contributed to the writing of the manuscript and study design. Z.S., Q.W. and P. H. contributed to critical data collection and analysis of the study. B. L. and L. S. contributed to the automated segmentation of chest CT. H. Z., H. Z., Y. L., Y. G., S. H., W. J., Y. L., J.M., L.M., X.W., M.W., M.S. contributed to enrolling patients with COVID-19.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The database used and analyzed in the present study is available from the corresponding author on reasonable request.

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