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Risk of in-hospital death associated with Covid-19 lung consolidations on chest computed tomography – A novel translational approach using a radiation oncology contour software☆

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ABSTRACT

Purpose: To determine whether the percentage of lung involvement at the initial chest computed tomography (CT) is related to the subsequent risk of in-hospital death in patients with coronavirus disease-2019 (Covid-19).
Materials and methods: Using a cohort of 154 laboratory-confirmed Covid-19 pneumonia cases that underwent chest CT between February and April 2020, we performed a volumetric analysis of the lung opacities. The impact of relative lung involvement on outcomes was evaluated using multivariate logistic regression. The primary endpoint was the in-hospital mortality rate. The secondary endpoint was major adverse hospitalization events (intensive care unit admission, use of mechanical ventilation, or death).
Results: The median age of the patients was 65 years: 50.6 % were male, and 36.4 % had a history of smoking. The median relative lung involvement was 28.8 % (interquartile range 9.5–50.3). The overall in-hospital mortality rate was 16.2 %. Thirty-six (26.3 %) patients were intubated. After adjusting for significant clinical factors, there was a 3.6 % increase in the chance of in-hospital mortality (OR 1.036; 95 % confidence interval, 1.010–1.063; $P = 0.007$) and a 2.5 % increase in major adverse hospital events (OR 1.025; 95 % confidence interval, 1.009–1.042; $P = 0.002$) per percentage unit of lung involvement. Advanced age ($P = 0.013$), DNR/DNI status at admission ($P < 0.001$) and smoking ($P = 0.008$) also increased in-hospital mortality. Older ($P = 0.032$) and male patients ($P = 0.026$) had an increased probability of major adverse hospitalization events.
Conclusions: Among patients hospitalized with Covid-19, more lung consolidation on chest CT increases the risk of in-hospital death, independently of confounding clinical factors.

1. Introduction

Lung consolidations in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are commonly visualized on radiological exams as ground-glass and diffuse patchy opacities [1–3]. Due to superior spatial resolution, these changes are usually better visualized by chest computed tomography (CT) instead of simple radiography [4,5].

Abbreviations: Covid-19, coronavirus disease-2019; DNR/DNI, do-not-resuscitate and do-not-intubate status; ICU, intensive care unit; IQR, interquartile range; OR, Odds Ratio; PACS, picture archiving and communication system; ROC, receiver operating characteristics; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Previous studies have indicated that imaging findings provide relevant information to establish diagnosis of coronavirus disease-2019 (Covid-19) at multiple stages of the disease [6–9]. Subsequent reports suggested a qualitative association between diffuse lung involvement and worse clinical outcomes [10–12], but the magnitude of the increase in the probability given any amount of lung infiltrates at admission is still to be determined.

It is postulated that the reduction in the amount of gas exchange in the consolidation areas, as a result of the combined effect of viral infection and host defense [13], plays a central role in the physiopathology of the Covid-19. In this setting, we hypothesize that by proportionally reflecting lung parenchyma impairment, the quantity of opacities relative to the total lung volume may be used to predict the need for more intensive medical care and survival. We therefore conducted a study relating the percentage of lung involvement by consolidations at the initial CT to the subsequent risk of adverse clinical outcomes.

2. Materials and methods

2.1. Study population

We screened all consecutive chest CT scans performed between February 1st, 2020, and April 17th, 2020, at two campuses of Michigan State University (Ascension Providence Southfield and Novi, MI, US). Cases with symptoms of viral pneumonia and confirmed by reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 from nasopharynx swabs were retrospectively selected. Patients who had their first CTs performed after intensive care unit (ICU) admission or intubation (n = 21) were excluded. Finally, four patients transferred to other institutions were excluded (**eFig. 1 in the Supplementary Appendix**). The present study was approved by the Ascension Providence Hospital Institutional Review Board (IRB number 1596627-1). Only retrospective deidentified information was used, and informed consent was waived.

2.2. CT Protocol and volumetric data

Nonenhanced chest CT scans from the lung apex to the bilateral costophrenic angles were performed in the feet-first and supine positions, using a 64-slice scanner (GE LightSpeed Volume CT, General Electric Healthcare, Chicago, Illinois, US). The breathing-hold technique was used. The acquisition was executed with 120 kV (tube voltage) and ~750 mA (Smart mA; tube current), and the image data sets were reconstructed with 1.25-mm slice thickness. There were no specific institutional recommendations regarding the indication for chest CT.

After the case selection stage, the images of the initial CT were transferred from the radiology picture archiving and communication system (PACS) to the radiotherapy treatment planning software (Eclipse Treatment Planning System - Version 15.6; Varian Medical Systems, Palo Alto, CA, US). We choose radiation oncology software due to the enhanced structure delineation capability in three planes (axial, coronal and sagittal), real-time tridimensional reconstruction, and the precision of the volumetric measurement tools. The structure contours (consolidations and lungs) for all cases were performed independently by two radiation oncologists with 5 years and 10 years of experience and familiarity with the contour interface who were blinded to the clinical endpoints. Discordances on final contours were resolved by consensus. The consolidations were analyzed and contoured using the lung window (-1000 to 0 Hounsfield units). Cases with massive peripheral opacities required alternating to the soft tissue window (-125 to 225 Hounsfield units) for better delineation of the lung-chest wall interface. Areas of emphysema and pleural effusion were not included in the normal lung and consolidation contours, respectively. The relative consolidation volume was calculated by dividing the volume of the lung consolidations measured in cubic centimeters by the total bilateral lung volume measured in cubic centimeters (**eTable 1 in the Supplementary Appendix**).

2.3. Statistical Analysis

The primary endpoint was the in-hospital mortality rate. The secondary composite endpoint was major adverse hospitalization events, defined as admission to the ICU, use of mechanical ventilation or in-hospital death. Patients with do-not-resuscitate and do-not-intubate status (DNR/DNI) at admission were included in the primary analysis but excluded from the composite outcome analysis. The study period encompassed the first two months of the pandemic in the state of Michigan (US). At that time, the institutional treatment protocol indicated that azithromycin, hydroxychloroquine, systemic corticoids, vitamin C and vitamin D would be offered to all patients admitted if there were no specific contraindications. Since therapy was uniform, treatments were not included as independent variables. Additional details on the patient's treatment are provided in **eTable 2 in the Supplementary Appendix**.

Qualitative variables are presented as absolute and relative frequencies. Quantitative variables are presented as medians and interquartile ranges (IQRs). The previous coexisting diseases analyzed were hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease, asthma/bronchitis, obstructive sleep apnea, coronary artery disease, stroke/transient ischemic attack, chronic kidney disease, cancer, acquired immunodeficiency syndrome, hepatitis B/C, and tuberculosis.

Initially, the possible association between the independent and dependent (outcomes) variables was quantified using the odds ratio estimated by a simple logistic regression model (Table 1 and **eTable 3 in the Supplementary Appendix**). To limit the number of variables in the multivariate model, only the variables with P-values < 0.1 in the simple logistic regression model were selected for the initial multivariate model. The final model was obtained using the backward stepwise method (likelihood ratio). Variables were removed from the model if they were not significant and did not act as confounders (change in β coefficient >20 %). The assumption of linearity was assessed for all continuous variables. No imputation method was used for missing data. The assessment of model significance and performance was performed by means of the Hosmer-Lemeshow goodness-of-fit test, receiver operating characteristics (ROC) curve and c-statistic, which represents the area under the ROC curve (AUC) (e**Fig. 2AB in the Supplementary Appendix**). Continuous variables could be categorized to achieve the model with the best replication potential based on Nagelkerke's R-squared and Hosmer-Lemeshow test. The factors associated with the outcomes at the respective final models were represented in a Cartesian coordinate system with percentage of lung consolidations (X axis) and probability of the outcome (Y axis). The significance level of the tests was fixed at 0.05 (two-sided). All analyses were performed using the MASS, ResourceSelection and pROC packages implemented in R software version 3.5 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Characteristics of the patients

One hundred fifty-four patients with laboratory-confirmed diagnoses of SARS-CoV-2 infection who underwent chest CT met the study inclusion criteria. The male-to-female ratio was 1:1. The median age of the patients was 65 years (interquartile range, 53–74), and the median body mass index was 31.1 kg/m^2 (interquartile range, 26.9–35.7). One-third of the patients had a history of smoking or were currently smoking. The median number of comorbidities was 3 (interquartile range, 1–4). Seventeen patients (11.0 %) had DNR/DNI status at admission. Other patient characteristics are presented in the Table 1 and **eTable 2 in the**

Supplementary Appendix.

Chest CT scans were obtained within 2 days from admission in 128 (83 %) of the cases. In 26 cases, the exam was performed between 2 days and 1 week (16.8 %) after admission, and in 1 case, the exam was performed on hospitalization day 10. Regarding radiological findings, 85.1 % of the patients had involvement of all five lung lobes, and only six cases (3.9 %) presented with pleural effusion. The median total bilateral lung volume was 3034.0 cubic centimeters (interquartile range, 2491.0–3581.0), and the median absolute consolidation volume was 787.5 cubic centimeters (interquartile range, 304.7–1464.2). The median percentage of consolidations relative to the total lung volume was 28.8 % (interquartile range 9.5–50.3).

3.2. Clinical Outcomes

At the time of analysis, all patients completed the hospitalization and were discharged after recovery of SARS-CoV-2 pneumonia or death. The last patient event (death) occurred 47 days after his initial CT sim, on May 30th, 2020.

Overall, the median hospitalization length from admission was 9

Table 1
Characteristics of the Patients in the Study at the Time of the Chest Computed Tomography and Association between the Characteristics and the Subsequent Event of In-Hospital Death. IQR: interquartile range. DNR/DNI: do-not-resuscitate and do-not-intubate status.

Characteristic	All Patients (N = 154)	Discharged Alive (N = 129)	Died During Hospitalization (N = 25)	Odds Ratio (95 % Confidence Interval)	P-Value
Age - Median (IQR)	65.2 (53.6–74.2)	63.2 (51.1–70.0)	79.6 (76.1–82.6)	1.157 (1.091–1.226)	<0.001
Age - N (%)					
≤65	76 (49.4)	75 (58.1)	1 (4%)	Reference	
>65	78 (50.6)	54 (41.9)	24 (96.0)	33.33 (4.375–253.989)	0.001
Sex - N (%)					
Female	76 (49.4)	66 (51.2)	10 (40.0)	Reference	
Male	78 (50.6)	63 (48.8)	15 (60.0)	1.571 (0.657–3.756)	0.309
Body-mass index - Median (IQR) - kg/m^2*	31.1 (26.9–35.7)	31.6 (27.1–37.5)	27.9 (25.7–31.8)	0.928 (0.869–0.992)	0.027
Smoking status - N (%)					
Never	96 (62.3)	89 (69.0)	7 (30.4)	Reference	
Former or current	56 (36.4)	40 (31.0)	16 (69.6)	5.086 (1.941–13.327)	0.001
Unknown	2 (1.3)				
Number of previous coexisting disease - Median (IQR)¶	3.0 (1.0–4.0)	2.0 (1.0–4.0)	4.0 (3.0–5.0)	1.402 (1.096–1.792)	0.007
Symptoms - N (%)					
Fever					
No	72 (46.8)	59 (45.7)	13 (52.0)	Reference	
Yes	82 (53.2)	70 (54.3)	12 (48.0)	0.778 (0.330–1.834)	0.566
Shortness of breath					
No	32 (20.8)	22 (17.1)	10 (40.0)	Reference	
Yes	122 (79.2)	107 (82.9)	15 (60.0)	0.308 (0.123–0.776)	0.012
Altered mental status					
No	137 (89.0)	117 (90.7)	20 (80.0)	Reference	
Yes	17 (11.0)	12 (9.3)	5 (20.0)	2.437 (0.775–7.667)	0.128
DNR/DNI at admission - N (%)					
No	137 (89.0)	124 (96.1)	13 (52.0)	Reference	
Yes	17 (11.0)	5 (3.9)	12 (48.0)	22.892 (6.968–75.211)	<0.001
Pleural effusion - N (%)					
No	148 (96.1)	124 (96.1)	24 (96.0)	Reference	
Yes	6 (3.9)	5 (3.9)	1 (4.0)	1.033 (0.116–9.243)	0.977
Involved lobes - N (%)					
<5	23 (14.9)	22 (17.1)	1 (4.0)	Reference	
5	131 (85.1)	107 (82.9)	24 (96.0)	4.935 (0.634–38.421)	0.127
Total bilateral lung volume - Median (IQR) - cm^3	3034.0 (2491.0–3581.0)	3005.1 (2517–3551)	3215.2 (2083.2–4020.4)	–	–
Absolute normal lung volume - Median (IQR) - cm^3	2081.2 (1323.8–2931.7)	2152.8 (1357.9–2983.7)	1700.5 (1093.1–2584.2)	–	–
Median relative normal lung volume (IQR) - %§	71.2 (49.3–90.9)	72.27 (52.07–92.47)	57.08(40.37–82.11)	–	–
Absolute consolidations volume - Median (IQR) - cm^3	787.5 (304.7–1464.2)	743.8 (267.9–1366.4)	1269.1 (508.2–1878.7)	–	–
Relative consolidations volume - Median (IQR) - %†	28.8 (9.5–50.3)	27.7 (7.6–49)	42.9 (17.9–59.7)	1.017 (1.001–1.034)	0.043

* The body-mass index = weight in kilograms divided by the square of the height in meters.

¶ From a 13-point scale which includes active or history of: hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease, asthma/bronchitis, obstructive sleep apnea, coronary artery disease, stroke/transient ischemic attack, chronic kidney disease, cancer, acquired immunodeficiency syndrome, hepatitis B/C, and tuberculosis.

§ Median relative normal lung volume = volume of normal lung in cubic centimeters divided by the total bilateral lung volume in cubic centimeters.

† Median relative lung consolidations volume = volume of the lung consolidations in cubic centimeters divided by the total bilateral lung volume in cubic centimeters.

days (interquartile range, 5–14). During the hospital stay, forty-five (32.8 %) required treatment at the ICU, and thirty-six (26.3 %) were intubated to receive mechanical ventilation. The median ICU length was 9 days (interquartile range, 5.5–15.5). Twenty-five patients died, resulting in an overall in-hospital mortality rate of 16.2 %. The in-hospital mortality rate was 28.9 % for the patients admitted to the ICU and 36.1 % if mechanical ventilation was used (Table 2).

3.3. Factors associated with outcomes

The median relative consolidation volumes were 42.9 % for the patients who died and 27.7 % for the patients who survived (OR 1.017 [1.001−1.034]; P = 0.043) (Table 1). In the final multivariate logistic regression model, patients with greater lung involvement (P = 0.007), who were older than 65 years (P = 0.013), who had a smoking history (P = 0.008), or were DNR/DNI status (P < 0.001) had a greater chance of in-hospital death (Table 3). Each unit of percent increase in lung consolidation increased the chance of in-hospital death by 3.6 % (OR 1.036; 95 % confidence interval, 1.010–1.063; P = 0.007). Fig. 1 presents the probability of in-hospital death for four subgroups of full-code patients (older than 65 years of age with and without a smoking history, and younger than 65 years of age with and without a smoking history).

The quantity of lung consolidations relative to the lung volume was also independently associated with major adverse hospitalization events (P = 0.002), with an increase of 2.5 % (OR 1.025; 95 % confidence interval, 1.009–1.042; P = 0.002) in the chance per additional unit of percent lung involvement (Table 3). Other factors associated with an increased risk of major adverse hospital events were advanced age (P = 0.032) and male sex (P = 0.026).

Fig. 2 provides axial images at the level of the carina and the respective tridimensional reconstruction of chest CTs of four cases with different percentages of lung involvement (A/a: 9.2 %; B/b: 29.7 %; C/c: 55.5 %; D/d: 83.1 %). Patients A/a and B/b had no major adverse hospitalization events and were discharged alive. Patient C/c survived after requiring ICU admission (7 days) and mechanical ventilation. Patient D/d did not survive after 47 days at the hospital, 32 days at the ICU, with mechanical ventilation support.

Table 2
Clinical Outcomes. CT: computed tomography. IQR: interquartile range. ICU: intensive care unit. DNR/DNI: do-not-resuscitate and do-not-intubate status.

Outcomes	Values
Admission to discharge (all) - median (IQR) - days	9.0 (5−14)
Admission to discharge (survivors) - median (IQR) - days	8 (5−14)
Admission to CT - median (IQR) - days	0.0 (0−1)
CT to discharge (all) - median (IQR) - days	8.0 (5−14)
CT to discharge (survivors) - median (IQR) - days	7 (4.5−14)
ICU admission	
no. / no. total (%)	45/137 (32.8)
Median length of stay (IQR) - days	9 (5.5−15.5)
Use of mechanical ventilation (intubation)	
no. / no. total (%)	36/137 (26.3)
no. / no. admitted to ICU (%)	36/45 (80.0)
Median length (IQR) - days	8.5 (4.25−15)
Successful extubation - no. / no. total (%)	23/36 (63.9)
Died in hospital[†]	
Overall - no. / no. total (%)	25/154 (16.2)
Non-ICU patients (excluding DNR/DNI) - no. / no. total (%)	0/92 (0.0)
Non-ICU patients (including DNR/DNI) - no. / no. total (%)	12/109 (11.0)
ICU patients - no. / no. total (%)	13/45 (28.9)
Intubated patients - no. / no. total (%)	13/36 (36.1)
Major adverse hospitalization event[*,‡]	
no. / no. total (%)	45/137 (32.8)

[*] Major adverse hospitalization event (secondary composite end point) included admission to intensive care unit, intubation for mechanical ventilation, or death.
[†] primary outcome.
[‡] secondary outcome.

4. Discussion

Since the initial case in January 2020 [14], more than 18 million individuals have been diagnosed with Covid-19 in the United States [15]. There have been over three hundred thirty thousand deaths, and a higher number of individuals have developed severe disease, requiring escalated medical care involving hospitalization, admission to the ICU, and the use of mechanical ventilation. During the peak phase of the pandemic in the state of Michigan (March-April 2020) [15], medical resources were used towards the maximum, raising the problem of resource allocation in situations of mass critical care demand [16–18]. In this scenario, tools to predict outcomes would be important to better triage patients who require more intensive support. On the other hand, patients who had a limited risk of developing major adverse events could be managed in a lower complexity facility or from home.

The present study indicated a quantitative increase in mortality and major adverse hospital events with more lung consolidations detected by CT in the setting of SARS-CoV-2 pneumonia. Each unit of percentage increase in lung involvement with consolidations increased the chance of in-hospital mortality by 3.6 % and the chance of major adverse hospital events by 2.5 %. Important information to better predict prognosis and guide clinical management can be derived from our findings. For example, a patient who is more than 65 years of age and has a history of smoking has a 15 % risk of dying during hospitalization if 10 % of the lung is involved at the initial assessment. That risk would escalate to 50 % for a similar patient with 60 % of lung involvement.

The clinical outcomes observed in our cohort were in line with experiences from other geographical areas. Eighty percent (36/45) of the cases admitted to the ICU in our series required mechanical ventilation, similar to the experiences from Seattle (US; 75 %, 18/24) [1], Lombardy (Italy; 88 %, 1150/1300) [19], and Wuhan (China; 64 %, 32/50) [20]. The ICU mortality in the present study (28.6 %,13/45) was also at the level found in the Italian data (26 %, 405/1581) [19] but lower than Seattle's experience (50 %, 12/24) [1]. The increased ICU mortality described in Seattle's case series could be related to more severe presentations, including patients with a higher percentage of lungs with opacities and late-stage disease (quantitative data were not provided by the authors). In addition, Seattle's surge occurred before the peak in Michigan's cases, which could explain differences in management, including the use of systemic corticoid (none versus 97.8 % on the ICU patients in our series) [21,22].

Of note, patients with do-not-resuscitate and do-not-intubate status at admission had twenty times higher chance of in-hospital mortality. It is unclear whether proceeding with mechanical ventilation or resuscitation maneuvers in those patients with low functional reserve would provide greater survival probability. In relation to cardiopulmonary resuscitation (CPR), previous experiences showed that less than 5 % of Covid-19 patients survived CPR after a cardiac arrest event [23,24]. Regarding mechanical ventilation, in the present study, two-thirds of the non-DNR/DNI (full-code) patients who required intubation recovered from respiratory insufficiency and were able to obtain a successful extubation.

Pleural effusions occurred in only 4% of the patients and were not associated to either endpoint. Other groups also reported a low incidence of pleural effusions [2,3], which could be related to exacerbation of other comorbidities instead of SARS-CoV-2 pneumonia. The other radiologic parameters, including absolute quantity of consolidations and the volume of nonaffected lung, were not used concomitantly as independent variables in the models due to their intrinsic relation with the percentage of lung involvement. Notwithstanding, a group from Piacenza (Italy) [25] indicated that cases with less well-aerated lung parenchyma on admission chest CT (< 73 % vs. > / = 73 %), per visual and

Table 3
Final Multivariate Logistic Regression Models for Primary and Secondary Outcomes. DNR/DNI: do-not-resuscitate and do-not-intubate status.

Death during hospitalization					
Variable	Category	Coefficient	SE	Odds Ratio (95 % Confidence Interval)	P-value
Age	≤65			Reference	
	>65	2.706	1.085	14.965 (1.785−125.466)	0.013
Smoking status	Never			Reference	
	Former or current	1.699	0.641	5.470 (1.558−19.204)	0.008
DNR/DNI at admission	No			Reference	
	Yes	2.991	0.843	19.907 (3.817−103.830)	<0.001
Relative lung involvement (%)*	Continuous	0.035	0.013	1.036 (1.010−1.063)	0.007
Intercept		−6.526	1.340		0.001
Major adverse hospital events					
Variable	Category	Coefficient	SE	Odds Ratio (95 % Confidence Interval)	P-value
Age	Continuous	0.033	0.015	1.033 (1.003−1.065)	0.032
Sex	Female			Reference	
	Male	0.898	0.404	2.455 (1.112−5.419)	0.026
Relative lung involvement (%)*	Continuous	0.025	0.008	1.025 (1.009−1.042)	0.002
Intercept		−4.164	1.118		<0.001

* Relative lung consolidations volume = volume of the lung consolidations in cubic centimeters divided by the total bilateral lung volume in cubic centimeters.

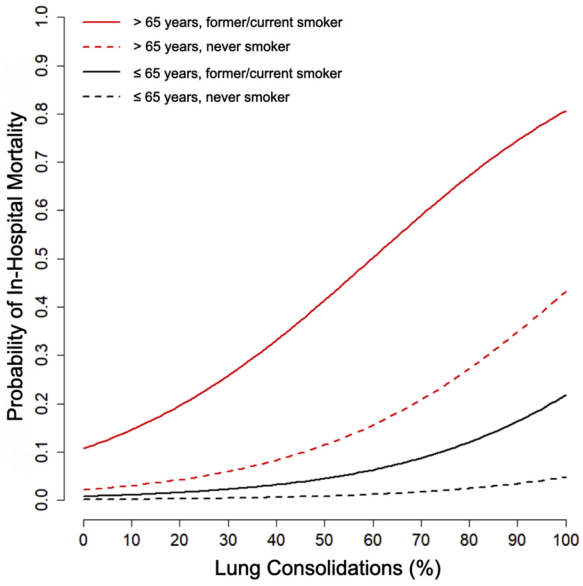

Fig. 1. Probability of in-hospital death per unit of percent lung involvement. Probability of in-hospital death (Y axis) per unit percent lung consolidations (X axis) for full code patients: older than 65 years of age and who were former or current smoker (solid red line); older than 65 years of age and no smoking history (dashed red line); 65 years of age or less and former/current smoker (solid black line); and 65 years of age or less and no smoking history (dashed black line). Primary outcome: Nagelkerke's R^2: 0.524. Hosmer-Lemeshow test: $\chi^2 = 9.213$; df = 8; P = 0.325.

software assessments, were associated with increased ICU use or death.

Our study limitations include the effect of changes in the total lung volume during respiratory cycle, which could interfere with the denominator of the percent lung involvement calculation. This source of uncertainty was partially controlled by instructing the patient to hold his or her breath during the CT scan acquisition, which also reduced the artifacts in the area of the lung-diaphragm interface. Further maneuvers such as sustained maximum inspiration would not be possible for dyspneic patients. In addition, alternative models incorporating the absolute consolidation volume as the independent variable confirmed our results (data not shown). Importantly, the model for in-hospital mortality was more accurate in predicting the death event when compared with the model for major adverse hospitalization events (**e**Fig **S2AB**), and both would benefit from external validation to minimize over-fitting bias. Another important limitation is the complexity of the infiltrate contour, which requires trained physicians and significant dedicated time. To illustrate this, videos of the contoured chest CTs of two cases are available online (**Video 1** and **Video 2**). The first presented with 0.2 % relative lung involvement that was contoured in less than ten minutes, and the second presented with 44.9 % relative lung involvement that required three hours to be completed. Further studies creating and validating artificial intelligence systems using neural network algorithms [26–29] could facilitate large scale quantification of percentage lung parenchyma compromised.

5. Conclusions

There is a quantitative relationship between lung involvement with Covid-19 consolidations and clinical outcomes. Per unit percent of lung involved, there was a 3.6 % increase in the chance of in-hospital mortality and a 2.5 % increase in major adverse hospital events. Therefore, this study provides evidence that chest CT is an potential tool in guiding escalation or de-escalation of care in the hospital setting.

Ethical statement

The work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

The present study was approved by the Ascension Providence Hospital Institutional Review Board (IRB number 1596627−1). Only retrospective deidentified information was used, and informed consent was waived.

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Summary statement

The percentage of lung involvement by consolidations at the initial CT is related to the subsequent risk of in-hospital death, independently of other clinical parameters.

CRediT authorship contribution statement

Lucas G. Sapienza: Conceptualization, Methodology, Data curation, Formal analysis, Writing - original draft, Supervision, Project

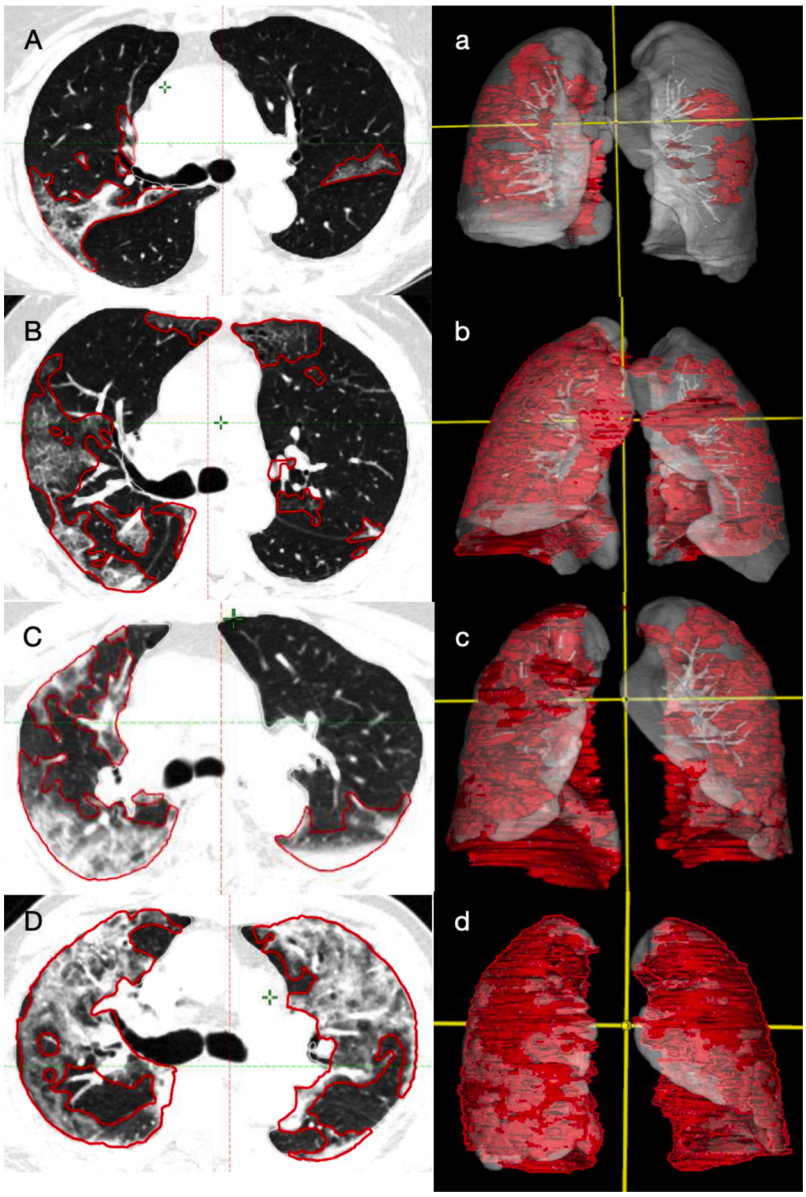

Fig. 2. Axial Chest CT Images (A-D) and Respective Tridimensional Reconstruction (a-d) of Four Patients with SARS-CoV-2.
Case A/a: 9.2 % lung involvement. 82 years-old female, full-code, former smoker. Estimated Probability of in-hospital death: 14.3 %. Estimated probability of major adverse hospital events: 22.3 %. Discharged after 3 days alive.
Case B/b: 29.7 % lung involvement. 73 years-old male, full-code, former smoker. Estimated Probability of in-hospital death: 25.6 %. Estimated probability of major adverse hospital events: 46.8 %. Discharged after 9 days alive.
Case C/c: 55.5 % lung involvement. 62.5 years-old female, full code, former smoker. Estimated Probability of in-hospital death: 5.4 %. Estimated probability of major adverse hospital events: 32.6 %. Discharged alive after 20 days alive (7 days in the ICU, 1 day of mechanical ventilation).
Case D/d: 83.1 % lung involvement. 79 years-old male, full-code, never smoker. Estimated Probability of in-hospital death: 29.5 %. Estimated probability of major adverse hospital events: 80.2 %. In-hospital death after 47 days (32 days in the ICU, 31 days of mechanical ventilation).

administration. **Karim Nasra:** Conceptualization, Methodology, Data curation, Writing - review & editing. **Vinícius F. Calsavara:** Conceptualization, Methodology, Formal analysis, Writing - original draft. **Tania B. Little:** Conceptualization, Writing - review & editing. **Vrinda Narayana:** Data curation, Software, Writing - review & editing. **Eyad Abu-Isa:** Conceptualization, Methodology, Data curation, Writing - original draft, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejro.2021.100322.

References

[1] P.K. Bhatraju, B.J. Ghassemieh, M. Nichols, et al., Covid-19 in critically ill patients in the Seattle region - Case series, N. Engl. J. Med. 382 (21) (2020) 2012–2022.
[2] M. Arentz, E. Yim, L. Klaff, et al., Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State, JAMA 323 (16) (2020) 1612–1614.
[3] C. Boa, X. Liu, H. Zhang, et al., Coronavirus disease 2019 (COVID-19) CT findings: a systematic review and meta-analysis, J. Am. Coll. Radiol. 17 (6) (2020) 701–709.
[4] H. Shi, X. Han, N. Jiang, et al., Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study, Lancet Infect. Dis. 20 (4) (2020) 425–434.
[5] W. Guan, Z. Ni, Y. Hu, et al., Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (18) (2020) 1708–1720.
[6] T. Ai, Z. Yang, H. Hou, et al., Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases, Radiology 196 (2) (2020) E32–E40.
[7] G. Herpe, M. Lederlin, M. Naudin, et al., Efficacy of chest CT for COVID-19 pneumonia in France, Radiology (2020), https://doi.org/10.1148/radiol.2020202568.

[8] M. Debray, H. Tarabay, L. Males, et al., Observer agreement and clinical significance of chest CT reporting in patients suspected of COVID-19, Eur. Radiol. (2020), https://doi.org/10.1007/s00330-020-07126-8.
[9] D. Nevens, C. Billiet, R. Weytjens, et al., The use of simulation-CT's as a coronavirus disease 2019 screening tool during the severe acute respiratory syndrome coronavirus 2 pandemic, Radiother. Oncol. (151) (2020) 17–19.
[10] Z. Zhou, D. Duo, C. Li, et al., Coronavirus disease 2019: initial chest CT findings, Eur. Radiol. 30 (8) (2020) 4398–4406.
[11] E. Guillo, I.B. Gomez, S. Dangeard, et al., COVID-19 pneumonia: diagnostic and prognostic role of CT based on a retrospective analysis of 214 consecutive patients from Paris, France, Eur. J. Radiol. 131 (2020), 109209, https://doi.org/10.1016/j.ejrad.2020.109209.
[12] A. Bernheim, X. Mei, M. Huang, et al., Chest CT findings in coronavirus disease-10 (COVID-19): relationship to duration of infection, Radiology 295 (3) (2020), 200463.
[13] M.Z. Tay, C.M. Poh, L. Rénia, P.A. MacAry, L.F.P. Ng, The trinity of COVID-19: immunity, inflammation and intervention, Nat. Rev. Immunol. 20 (6) (2020) 363–374.
[14] M.L. Holshue, C. DeBolt, S. Lindquist, et al., First case of 2019 novel coronavirus in the United States, N. Engl. J. Med. 382 (10) (2020) 929–936.
[15] CDC – National Center for Health Statistics – CDC COVID Data Tracker, 2020. November 26, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrends.
[16] R.C. Maves, J. Downar, J.R. Dichter, et al., Triage of scarce critical care resources in COVID-19 an implementation guide for regional allocation: an expert panel report of the Task Force for Mass Critical Care and the American College of Chest Physicians, Chest 158 (1) (2020) 212–225.
[17] V. Tambone, D. Boudreau, M. Ciccozzi, et al., Ethical criteria for the admission and management of patients in the ICU under conditions of limited medical resources: a shared international proposal in view of the COVID-19 pandemic, Front. Public Health 8 (2020) 284.
[18] T. Leclerc, N. Donat, A. Donat, et al., Prioritisation of ICU treatments for critically ill patients in a COVID-19 pandemic with scarce resources, Anaesth. Crit. Care Pain Med. 39 (3) (2020) 333–339.
[19] G. Grasselli, A. Zangrillo, A. Zanella, et al., Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy, JAMA 323 (16) (2020) 1574–1581.
[20] F. Zhou, T. Yu, R. Du, et al., Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, Lancet 395 (10229) (2020) 1054–1062.
[21] RECOVERY Collaborative Group, P. Horby, W.S. Lim, J.R. Emberson, et al., Dexamethasone in hospitalized patients with Covid-19 - preliminary report, N. Engl. J. Med. (July 17) (2020), NEJMoa2021436, https://doi.org/10.1056/NEJMoa2021436.
[22] WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis, JAMA (September 2) (2020), e2017023.
[23] F. Shao, S. Xu, X. Ma, et al., In-hospital cardiac arrest outcomes among patients with COVID-19 pneumonia in Wuhan, China, Resuscitation 151 (2020) 18–23.
[24] S.B. Thapa, T.S. Kakar, C. Mayer, D. Khanal, Clinical outcomes of in-hospital cardiac arrest in COVID-19, JAMA Intern. Med. (September 28) (2020), https://doi.org/10.1001/jamainternmed.2020.4796.
[25] D. Colombi, F.C. Bodoni, M. Petrini, et al., Well-aerated lung on admitting chest CT to predict adverse outcome in COVID-19 pneumonia, Radiology 296 (2) (2020) E86–E96.
[26] A.M. Turing, Computing machinery and intelligence, Mind 49 (1950) 433–460.
[27] T.D. Pham, A comprehensive study on classification of COVID-10 on computed tomography with pretrained convolutional neural networks, Sci. Rep. 10 (2020) 16942.
[28] A.A. Ardakani, A.R. Kanafi, U.R. Acharya, N. Khadem, A. Mohammadi, Application of deep learning technique to manage COVID-19 in routine clinical practice using CT images: results of 10 convolutional neural networks, Comput. Biol. Med. 121 (2020), 103795.
[29] J. Mushtaq, R. Pennella, S. Lavalle, et al., Initial chest radiographs and artificial intelligence (AI) predict clinical outcomes in COVID-19 patients: analysis of 697 Italian patients, Eur. Radiol. (2020), https://doi.org/10.1007/s00330-020-07269-8.