CT scores predict mortality in 2019-nCoV pneumonia

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Abstract

Background: While 2019-nCoV nucleic acid swab tests has high false positives rate, How to diagnose 2019-nCoV pneumonia and predict prognosis by CT is very important.

Methods: In this retrospective single-center study, we consecutively included suspected 2019-nCoV pneumonia critical cases in the intensive care unit of Wuhan third hospital from January 31, 2020 to February 16, 2020. The cases were confirmed by real-time RT-PCR, and all patients were evaluated with CT, cutoff values were obtained according to the Yoden index, and were divided into high CT score group and low CT score group. Epidemiological, demographic, clinical, and laboratory data were collected.

Results: The major imaging feature of 2019-nCoV pneumonia is the ground glass opacity (GGO). Multivariate regression analysis found that CT score and absolute count of lymphocytes were independent risk factor for death, and CT score predicted mortality AUC-ROC =0.7, cutoff=1.45. When the absolute count of lymphocytes decreased, the patient's CT also deteriorated.

Conclusion: CT score and absolute count of lymphocytes were independent risk factor for death, and patients with high CT score may have a worse prognosis. Lower absolute count of lymphocytes may indicated the patient's CT also deteriorated.

Introduction

In December 2019, pneumonia associated with the 2019 novel coronavirus (2019-nCoV) was reported in Wuhan, China. Between 4% and 11% of patients with 2019-ncov pneumonia rapidly develop acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications within a short period of time, and eventually deteriorate and die from multiple organ failure[1, 2].

Computed tomography (CT) examinations, which are reproducible and objective, will be

used clinically to determine the severity of pneumonia and will constitute an effective tool for defining accurate management. Several studies have reported a relationship between high-resolution CT and the prognosis of pulmonary fibrosis, and have found that radiographic fibrosis scores based on HRCT scan reticulation and honeycomb degree predict mortality [3, 4]. However, the relationship between CT and the prognosis of 2019-nCoV pneumonia remains unknown.

While 2019-nCoV nucleic acid swab tests had up to 41 percent false positives, and lung CT abnormalities were detected in 74%t of 2019-nCoV cases[6].In this study, we retrospectively analyzed patients with suspected 2019-nCoV pneumonia to assess whether imaging CT scores were useful predictors of mortality.

Methods

Study design and participants

For this retrospective single-center study, we continuously collected patients with suspected 2019-nCoV pneumonia in the intensive care unit, Wuhan third hospital, China on January 31, 2020 and February 16, 2020. The study was approved by the ethics committee and exempted from written informed consent.

Inclusion criteria: all patients suspected of 2019 novel coronavirus infection.

Exclusion criteria: patients’ data are not available.

Collection data

We obtained epidemiological, demographic, clinical, laboratory, management and outcome data from patients’ records. Clinical results were followed up until February 16, 2020.

Swabs of the upper respiratory tract from all patients at admission were kept in viral transport media. Real-time RT-PCR was used to detect 2019-nCoV. All patients underwent chest CT examination.

Collect all of the patients radiographic features include: ground glass opacity(GGO),

consolidation, and pleural effusion, seepage, and involvement of leaf number. According to the acute exacerbation of idiopathic pulmonary fibrosis score (AE - IPF) rating of each patient chest CT[3]. Two physicians for the patients with chest CT image analysis and calculation of each layer, CT score = normal lung tissue (%) × 1 + GGO (%) × 2 + consolidation (%) × 3. Finally, the scores of all levels were averaged to get the final score, and using the higher score by two physicians scored. The clinical case and outcome of the patient cannot be consulted during the scoring process.

Our treatment plan: the antiviral drug was Abidole, Moxifloxacin was the initial antibiotic, the antibiotic was adjusted according to the culture result, the anticoagulant therapy was adopted according to the condition .When absolute count of lymphocytes $\square 0.5*10^9$/L, intravenous immunoglobulin was given for 5 days, at the same time the albumin was supplemented, after 5 days the absolute number of lymph node was still low, thymosin was added to enhance the immune function. Small doses of hormone (1–2 mg/kg) for 3–5 days which depending on patient’s exudation .The rest of the treatment was based on guidelines of WTO[8]

Outcome

The primary outcome was the 7-day mortality .We also described the demographics; Physical signs on admission; Laboratory results; Chest CT score; and clinical outcomes.

Statistical analysis

If data were normally distributed, we represented the continuous measurements as the mean (SD), otherwise they were represented as the median (IQR), and the classification variables as counts (%). For laboratory results, we also evaluated whether the measurements were outside the normal range. Logistic regression analysis was used to evaluate the outcomes based on the risk factors selected through univariate analysis. The diagnostic value of CT score in predicting death was evaluated by calculating the area

under the receiver operating characteristic curve (AUC ROC). AUC ROC analysis was performed by comparing survivors with non-survivors. The optimal cutoff value was determined by the highest value of the Youden index calculated for sensitivity and specificity, as shown in the AUC ROC analysis. We used SPSS (version 26.0) for all analyses.

Results

The study included 39 patients with suspected 2019-nCoV. A total of 16 (41%) tested positive for the nucleic acid of 2019-nCoV virus. Of these, 24 (61.5%) were male, with an average age of 60 years (51–66)(Table 1). At admission, 14 (35.9%) of the patients had tachypnea. Platelets were lower than normal in 2 cases (5.13%) and higher than normal in 1 case (2.56%). Three patients (7.69%) had abnormal liver function. 4 (10.25%) abnormal renal function. 3 cases (7.69%) had abnormal myocardial enzyme spectrum. In most patients, D-Dimer were greater than 35 mg/L during the course of disease.

Table 1

Demographic characteristics, baseline characteristics, and clinical outcomes of patients with suspected novel coronavirus infected

	All patients n = 39	High-CT score n = 25	Low-CT score n = 14	P value
Age,years	60(51–66)	60(51–64)	62.5(40.25–78.75)	0.768
Sex				
Men	24(61.5)	16(64)	8(57.1)	0.740
Women	15(38.5)	9(36)	6(42.9)	0.740
Symptoms				
Fever%	36 (92.3)	24(96)	12(85.7)	0.289
Respiratory rate	26(22–40)	35(23.5–44)	24(19.75-26)	0.007*
≥24breaths per min	14(35.9)	11(44)	3(21.4)	0.187
Systolia pressure,mmHg	130(130–147)	135.5(123.5–147)	124(116–148)	0.308
SpO_2,%	93(84–97)	91(81.75–95.75)	93(85-97.75)	0.947
Heart rate	95(86–100)	95(86–100)	94(92.25-113.75)	0.467
Laboratory test				
White blood cell count,$\times 10^9$/L	8.6(5.12–10.8)	8.6(5.275–11.7)	8.35(3.2-9.975)	0.247
Neutrophil %	88.9(81.2–91.7)	88.85(82.92-91.925)	895(77.4–91.6)	0.26
Lymphocyte count,$\times 10^9$/L	0.48(0.33–0.685)	0.45(0.285–0.685)	0.58(0.43–0.75)	0.715
Lymphocyte %	6.36(4.1-11.82)	5.52(3.31–9.83)	8.43(5.03–17.45)	0.747
Platelet＜100 × 10^9/L, %	2(5.13)	1(4)	1(14.3)	1
D-dimer,mg/L	5.93(2.49–25.83)	6.41(2.725–33.75)	5.16(1.59–6.46)	0.261
Albumin,g/L	28.05(25.55–30.1)	25.6(22.65–28.42)	28.8(25.3–34.6)	0.751
Potassium,mmol/L	3.77(3.36–4.24)	3.78(3.4–4.22)	3.7(3.2–4.36)	0.662
Calcium,mmol/L	1.21(1.15–1.92)	1.87(1.15–1.92)	1.19(1.14–1.9)	0.431
Sodium,mmol/L	142(141–145)	142(140–144)	142.5(141-144.5)	0.971
Procalcitonin,ug/L	0.19(0.085–0.382)	0.335(0.11–0.74)	0.14(0.07–0.287)	0.080
C-reactive protein, mg/	59(21.39-143.79)	81.5(22.12–188.9)	58.69(15.81–70.88)	0.152
ph	7.41(7.375–7.438)	7.42(7.39–7.48)	7.4(7.33–7.41)	0.069
PaO_2,mmHg	58(49-150.5)	55.5(48.5–60.5)	151(56-234.25)	0.034
$PaCO_2$,mmHg	39.5(36.05–47.02)	38(31.85–46.05)	43.55(38.85-48.425)	0.338
Lac, mmol/L	2.23(1.137–3.68)	3.39(1.42–4.26)	2.2(0.75–2.432)	0.030
HCO_3^-	25.4(23.7-28.55)	25.7(23.55–28.62)	25.4(23.6–28.7)	0.952
Acute myocardial injury %	4(10.25)	3(12)	1(7.1)	1
Acute liver injury %	3(7.69)	2(8)	1(14.3)	1
Acute kidney injury %	4(10.25)	2(8)	2(14.3)	1
2019-nCoV Nucleic acid test positive%	16(41)	13(52)	3(21.4)	0.093
7 day mortality%	11(28.2)	11(44)	0	0.003*

*p＜0.05

Figure1 showed CT of 2019-nCoV pneumonia, A.Man,84-years-old,cough with fever more than 10 days, CT score 1.10 his 7-day mortality outcome was survival. B. Man,62-years-old， cough with fever more than 7 days, CT score 1.55, his outcome was survival. C. Woman，63-years-old，cough with fever for 7 days, CT score 1.7, her outcome was died. D. Woman,52-years-old,cough with fever for 10 days, aggravation with shortness of breath

for 5 days, CT score 1.95,her 7-day mortality outcome was died.

Our study found that GGO was the main manifestation of the 2019-nCoV pneumonia. The intense immune response of the body could quickly enter the progressive stage and develop into pulmonary consolidation, but pleural effusion was less frequent. Lymph node enlargement was also absent or insignificant, and cavities were less frequent.

When the elderly were weak or suffer from other basic diseases, such as diabetes and immunodeficiency, multiple pulmonary infections may occur. The CT findings were complex, and multiple signs may appeard. Severe pneumonia progressed rapidly, could appear diffuse bilateral lung consolidation (namely so-called "white lung"), but also accompanied by a small amount of pleural effusion. In this case, the diseased lungs rarely exchange gas, causing respiratory distress syndrome and suffocation.

From the peripheral lung zone to the diffuse distribution of GGO in the central lung region, it takes only 1 to 2 days for the rapid. Three days after the onset of this case, the disease developed rapidly, GGO and lung consolidation were not limited to the peripheral lung zone, and lesions in the central lung were also obvious, with bilateral diffuse distribution presenting a butterfly wing shape. After 14 days of onset, in addition to GGO, pulmonary consolidation, and bronchial gas equality signs, pulmonary interstitial fibrosis changes in the filaments and cords began to appear.

Death on day 7 was taken as the output item for binary Logistic regression analysis, and the P value of the above three variables were all less than 0.25, which led to multivariate binary Logistic regression analysis. The OR value of CT score was 10, and the P value was 0.003,(Table 2).

Table 2

Multivariate analysis of mortality risk (n = 39).

	OR	CI (95%)	P-value
Age	2.358	0.346–16.07	0.381
Male	2	0.436–9.176	0.373
2019-nCoV Nucleic acid test positive	1.288	0.315–5.267	0.725
CT score	10	1.125–88.91	0.003*
Lymphocyte count,×109/L	0.795	0.426–1.481	0.002*

*p□0.05

The distribution map of CT score of 39 cases has the characteristics of normal distribution, so the P value obtained by Person correlation analysis is 0. 003 < 0.05, showing a linear correlation between them. The area under the curve(AUC-ROC) was 0.7, the standard error was 0.082, and the 95% confidence interval (95%CI)was 0.539 ~ 0.860. According to the curve results, the case fatality rate increased when the CT score was greater than 1.45, as shown in Fig. 4.

According to whether the CT score was greater than 1.45, the patients were divided into high CT score group and low CT score group. In terms of symptoms, the rate of shortness of breath in the high CT score group was significantly higher than that in the low CT score group. In laboratory results, PaO2 was lower in the high CT score group, and serum lactic acid level was higher in the high CT score group. There was no significant difference in other laboratory results, and there was no significant difference in the positive rate of new coronavirus nucleic acid detection, but the 7-day mortality rate of high CT group was significantly higher than that of low CT group (Table 1).

Imaging Features of 2019 Novel Coronavirus (Table 3), CT images showed GGO distribution in the marginal areas of the lung in 14 cases, 25 cases were enlarged to the central area of the lung, and 16 cases were complicated with consolidation. As the follow-up time was short and no significant fibrosis was observed. The early stage was GGO, and pulmonary consolidation began at a median of 5 days, with no statistically significant difference between the two groups.

Table 3
Imaging Features of 2019 Novel Coronavirus

	High CT score n = 25	Low CT score n = 14	P-value
GGO in the limbic region of the lung	25(100%)	14(100%)	-
GGO expands to the central area of the lung	25(100%)	0	-
Consolidation	10(40%)	6(42.8%)	1
Time of GGO became pulmonary consolidation	5(4.75-6)	5(4.5–6.5)	0.860

In our study, when the absolute count of human lymphocytes decreased. The patient's CT also deteriorated. Figure 2 showed absolute count of lymphocytes and CT of a dead patient, man,51-years-old,cough with fever more than 10 days, nucleic acid test positive, absolute count of lymphocytes reduced progressively, CT performance also deteriorated, his 7-day mortality outcome was dead. Figure 3 showed absolute count of lymphocytes and CT of a survival patient, woman,49-years-old,cough with fever 6 days, nucleic acid test positive, absolute count of lymphocytes and CT both recovered gradually.

Discussion

This is an observational descriptive study of patients with suspected 2019-nCoV pneumonia, including data of 39 patients from the ICU of Wuhan third hospital from January 31 to February 16, 2020. It describes the CT of 2019-nCoV pneumonia and has scored and quantified the imaging findings.

Our study found that the nucleic acid positive rate (41%) of the suspected 2019-ncov was similar to that of previous studies [6], but patients with a single negative nucleic acid test could not be excluded from new coronavirus infection. In order to reduce nosocomial cross infection, it is urgently needed to detect multiple pathogens once in a short time in clinic, so as to quickly distinguish cold flu and 2019-nCoV population.

Most 2019-nCoV pneumonitis is mild/common viral pneumonia. Light very light or no clinical symptoms, but CT can have mild abnormalities, beginning mainly characterized by bilateral subpleural small piece of ground glass opaque light and shadow, ground glass

opacity(GGO), also can be in unilateral lung field. With symptoms and signs of normal cases CT performance similar to light, but quickly to GGO lung central extension, later with a consolidation of the lung (small flake and chamber nodules), with time delay and pulmonary interstitial changes, such as septal thickening and thickening of alveolar interval (pavement), lobular core, and a large increase in the number of bronchial pulmonary (lung) beam fuzzy, pleural thickening. The clinical symptoms of severe viral pneumonia progressed rapidly. CT showed that GGO gradually evolved from flaky lung consolidation with a wide range of lesions, accompanied by bronchial gas phase, increased blurring of lung texture, and a small amount of pleural effusion. Pulmonary cavity formation is rare and mediastinal lymph node enlargement is rare. A very small number of people may develop into critically ill cases with diffuse lesions in both lungs and even uniform extensive consolidation (" white lung "). A combination of multiple infections can also be more severe[12–15]. In our study, CT images showed GGO distribution in the marginal areas of the lung in 14 cases(low CT score group), 25 cases were enlarged to the central area of the lung(high CT score), and 16 cases were complicated with consolidation. As the follow-up time was short and no significant fibrosis was observed. The early stage was GGO, and pulmonary consolidation began at a median of 5 days.

We found that most of the patients in onset about a week or so weak CT to display the subpleural GGO, even some patients in the earlier CT or negative, weak without interstitial thickening of GGO instructions were fresh, but the fact is that this kind of GGO appear relatively long time after the symptomatic, later to become severe in hospital. Combined with mild cases and common cases are many, although the pharyngeal swab positive nucleic acid, I wonder if, like the common cold, some patients only infected with the upper respiratory tract self-limiting, only a few developed into pulmonary infection, even serious, dangerous patients. Beginning of upper respiratory tract infection, a few

progress, a large number of virus particles with breathing into pulmonary gas exchange area, namely, peripheral pulmonary and alveolar mucosa inflammation after adsorption mainly in the alveolar walls, which produce GGO, viral replication after more and stronger immune mechanism against epidemic diseases, inflammation, not just the liquid leakage, fibrous hyperplasia of seepage and gradually form paving stone), the consolidation of the lung, the late pulmonary fibrosis. In partial patient lung pathological changes are very apparent, but upper respiratory tract infection has absorbed, dry cough does not have phlegm, pharynx swab nucleic acid tests can be negative, false negative at this time.

CT score through visual measuring each layer of the proportion of CT image of pathological changes, the score method has been used to evaluate prognosis of idiopathic pulmonary fibrosis, there is no report using CT score to assess 2019 - nCoV pneumonia prognosis, some studies have found that a similar area of grading method to explore its relationship with viral pneumonia of viral load [7]. In our study,patients generally onset the disease 7 to 10 days ago, there was no significant difference in comorbidity and laboratory results, except for PaO_2 and Lac in blood gas analysis, there was no significant difference between the high CT score and low CT score groups at the initial level. Our study showed a higher 7-day mortality in high CT score group, indicating that the disease progressed more seriously in the later stages of a high CT score. At present, many cases of 2019-nCoV have occult onset, with one or even multiple negative nucleic acid tests and no clinical symptoms. However, CT images have been positive. These patients may cause familial aggregation infection[10], which further spreads the epidemic[11]. Therefore, it is necessary to suspect the diagnosis of 2019-nCoV in pneumonia patients with obvious abnormalities in CT. Of course, Guan et al. found that there might be normal radiological manifestations in some infected patients, and the accuracy rate of diagnosing neocoronavirus infection by CT alone was 76.4%[6]. We also need to combine clinical

manifestations with laboratory results.

We also observed a correlation between lymphoid counts and CT changes, absolute value of lymphocytes reduced progressively, CT performance also deteriorated. Most studies[1, 2, 6] found a decrease in lymphoid absolute count of 2019-nCoV patients. Low lymphoid absolute count may indicate the patient more severe and may get higher mortality. In our study, one dead patient lymphoid absolute count even was close to zero.

This study has several limitations. Firstly, this study is a single-center retrospective study. The number of studies is relatively small, and the next step is to include as many cases as possible in multiple centers to gain a more complete understanding of 2019-nCoV. Second, more information, especially about clinical outcomes, is not available for analysis. We suggest to observe whether there is a relationship between the speed of large GGO conversion to pulmonary consolidation and the later conversion to pulmonary fibrosis. However, the data in this study could provide an early assessment of CT findings for 2019-nCoV pneumonia in Wuhan, China.

Conclusion

In summary, in patients with suspected 2019-nCoV infection, higher CT scores may indicate the patient more severe and may get higher mortality. When the absolute count of lymphocytes decreased, the patient's CT also deteriorated. So we require close attention in combination with clinical manifestations and laboratory results.

Declarations

Acknowledgements

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Ethical Approval and Consent to participate

Ethics approval from Shanghai General Hospital Institutional Review Board: reference

number (2020[11]), Written informed consent was waived due to the rapid emergence of this infectious disease.

Consent for publication

All the authors have approved the manuscript and agree with publication.

Registration details

Trial registration: NCT04284046, ClinicalTrials.gov.

Availability of supporting data

After publication, the data will be made available to others on reasonable requests to the corresponding author.

Competing interests

We declare no competing interests.

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Authors' contributions

YX,YLU,DH,PH,YYT,TGW,,LQL,FSZ and RLW contributed to the study conception and design, analysis and interpretation of data; drafting of the article and critical revision for important intellectual content. All the authors have read and approved the final manuscript.

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Figures

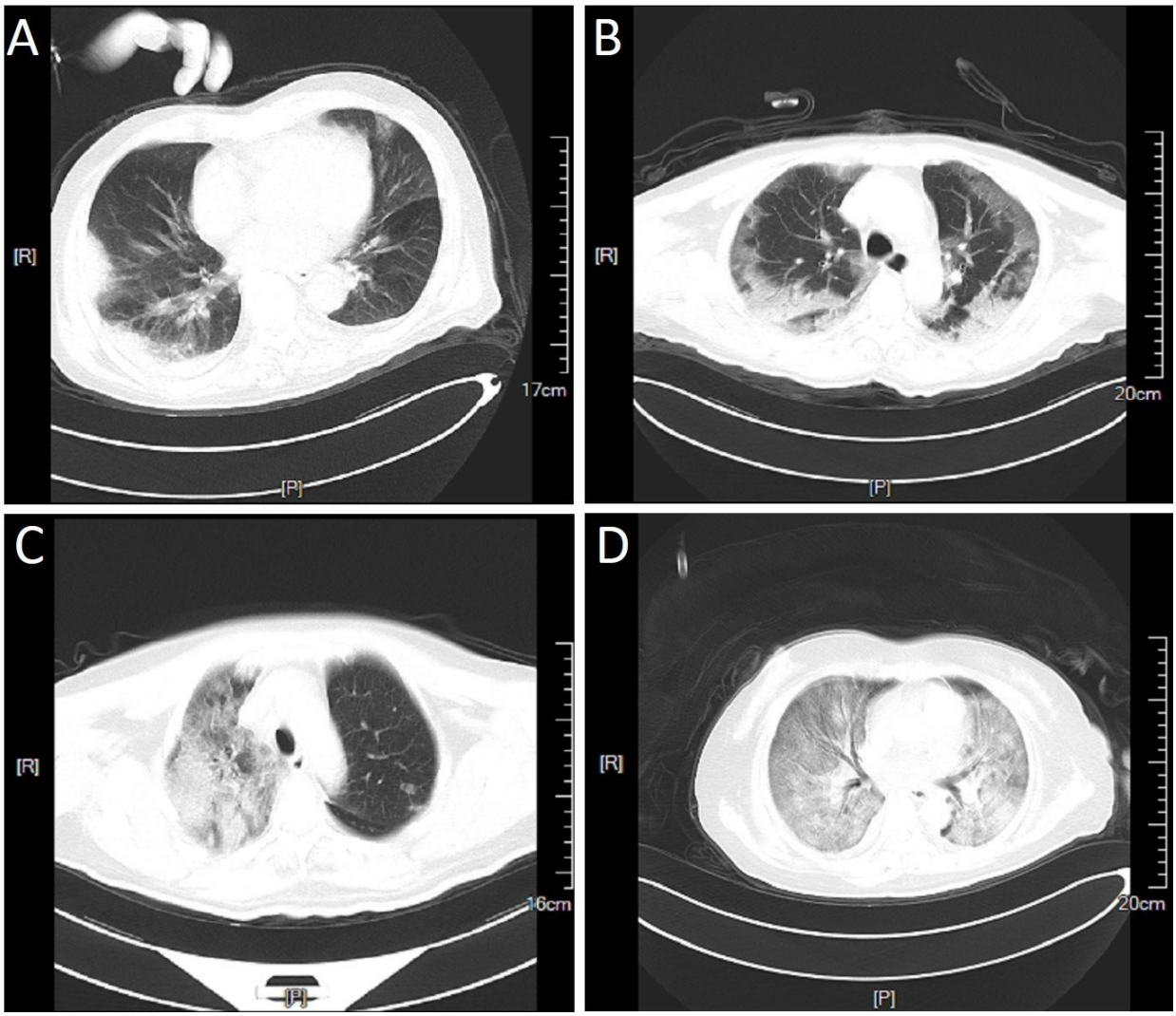

Figure 1

CT of 2019-nCoV pneumonia(A. Man，84-years-old，cough with fever more than 10 days, his outcome was survival. B. Man，62-years-old， cough with fever more than 7 days, his outcome was survival. C. Woman，63-years-old，cough with fever for 7 days, her outcome was died. D. Woman，52-years-old，cough with fever for 10 days, aggravation with shortness of breath for 5 days，her outcome was died.)

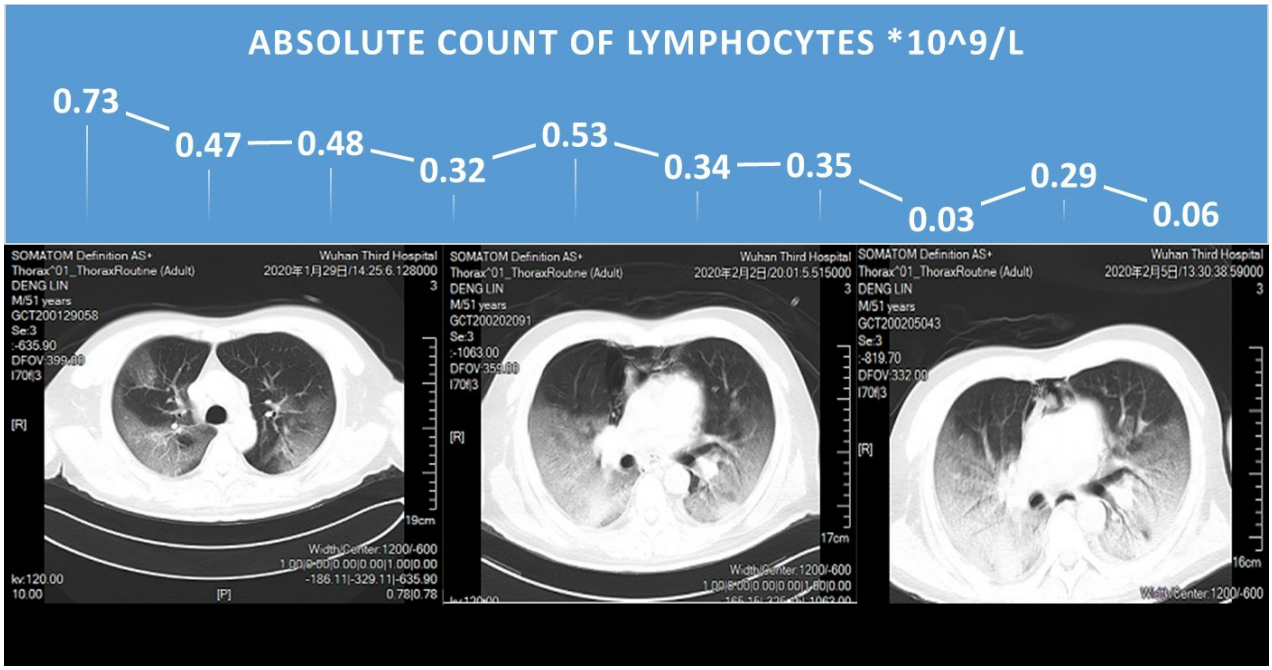

Figure 2

Absolute count of lymphocytes and CT of a dead patient

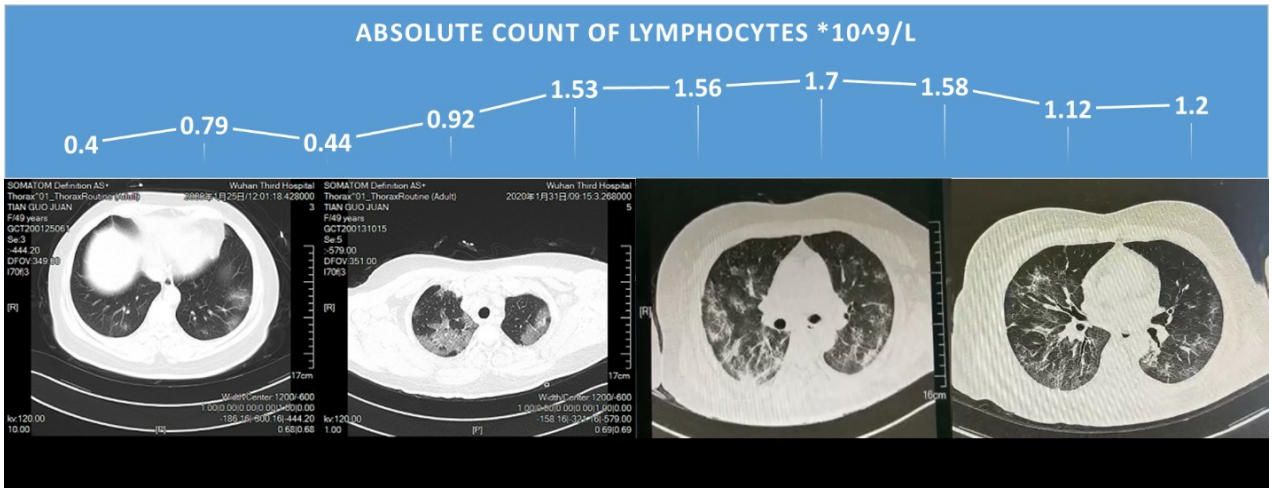

Figure 3

Absolute count of lymphocytes and CT of a survival patient

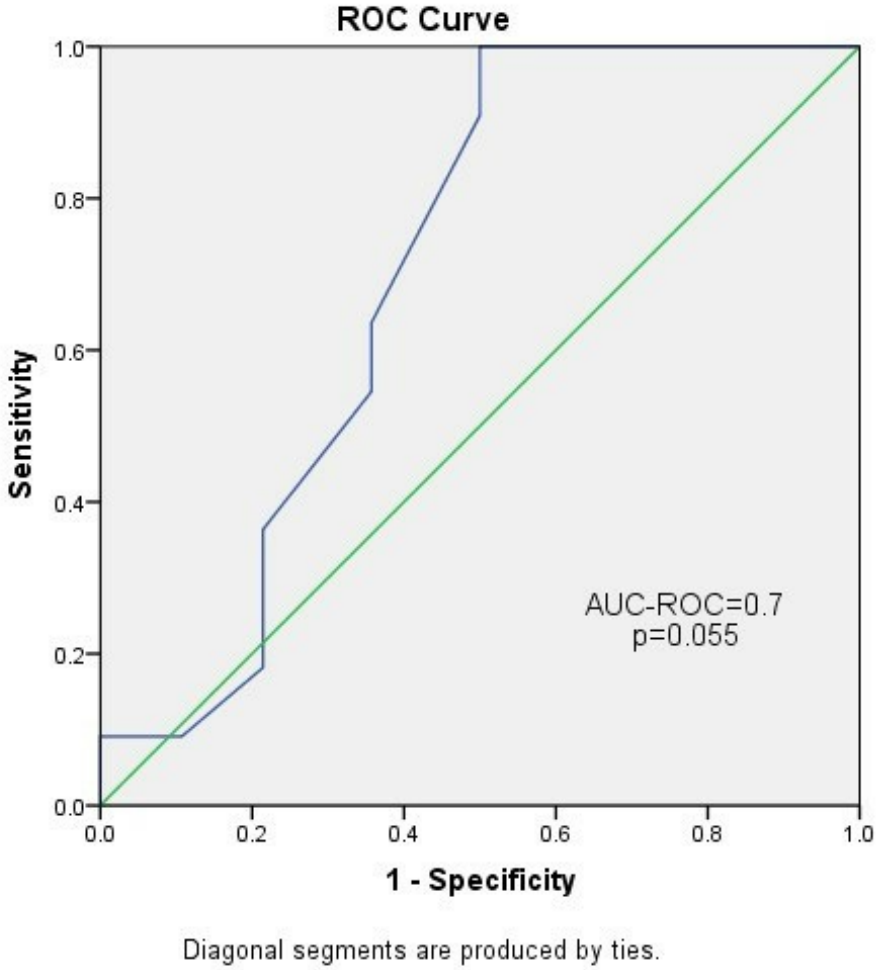

Figure 4

ROC analysis of the mortality based on CT score