Malignancy history had no marked effect on the prognosis of COVID-19: A cohort study

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Research

Keywords: COVID-19, malignancy, laboratory finding, survival, progression

Posted Date: July 20th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-44171/v1

Abstract

Background

Primary disease influenced the prognosis of coronavirus disease 2019 (COVID-19), but the clinical characters of patients accompanied with tumor were few reported.

Methods

We enrolled 528 COVID-19 patients. Date of laboratory tests and outcome were divided to corresponding groups to compare the risk factors of disease severity, progression and survival.

Results

The disease severity at hospitalization, progression rate (51.43% vs 54.42%) and mortality (19.51% vs 11.91%) were equal between tumor and non-tumor group. In both groups, lymphopenia was negatively related to the severity grading (OR = 0.019 and 0.168 separately), NLR was positively correlated with the poor outcome (OR = 1.371 and 1.155 separately), and CRP was relevant to the disease progression and survival (OR = 1.334 and 1.303 separately).

Conclusions

Malignancy history may have no marked effect on the severity and prognosis of COVID-19. Lymphopenia, NLR and CRP levels could be regarded as indicators to determine severe cases, and predict progression and survival.

Introduction

Since December 2019, the Wuhan city, in the center of China, was attacked by a novel coronavirus which was later designated as severe acute respiratory syndrome coronavirus 2, (SARS-CoV-2). This coronavirus Infect patients of all ages, exhibiting multiple systemic inflammations, included severe viral pneumonia with respiratory failure and even death, called coronavirus disease 2019 (COVID-19) by WHO[1–3] (Huang C, Chen N, Guan WJ). Until July 21th 2020, there were 12579569 confirmed cases of SARS-CoV-2 infection worldwide, including 559049 deaths[4].

With increasing understanding of this pandemic, a large amount of publications have precisely described the demographic, clinical features, illness severity grading and prognosis of COVID-19. Noteworthily, comorbidities were frequently present in 30–40% of patients, while the most common were hypertension, diabetes and coronary heart disease[5]. These comorbidities were confirmed as predictors to assess the clinical severities. Among which, malignancy was little mentioned and rarely reported, as their minor

proportion in hospitalized COVID-19 patients. As Guan at al. reported, together with chronic obstructive pulmonary disease (COPD), hypertension and diabetes, malignancy was one of the risk factors of disease severity[6]. While another Meta-analysis suggested that there was no correlation between malignant tumor and COVID-19 patients' aggravation[7]. Few studies only reported the epidemiological data or overall outcome of this particular population[8–10]. Here we focused on this minor population to explore the distinguishing laboratory feature in SARS-CoV-2 infected patients with tumor.

Methods

Study design and participants

This retrospective cohort study included 528 COVID-19 patients from February 5 to March 10, 2020, admitted to the Central Hospital of Wuhan, one of COVID-19 designated hospitals in Wuhan. The data cutoff is April 10, 2020. Patients diagnosed as COVID-19 according to Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia recommended by the National Health Commission(NHC) of China (version 7.0)[11] were included. The study was approved by The Central Hospital of Wuhan Hospital Ethics Committee and written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Data Collection

Demographic, clinical, laboratory and outcome data were extracted from electronic medical records using a standardized data collection form. All data were collected by experienced clinicians and checked by two researchers independently.

Procedures

SARS-CoV-2 infection was confirmed by positive next-generation sequencing or real-time RT-PCR methods of respiratory specimens as previously described[12]. Routine laboratory examinations included blood examinations, coagulation and biochemical tests. The clinical outcomes were evaluated by two experienced clinicians.

Definitions

The disease severity of COVID-19 was defined according to the guideline of Chinese NHC[11]. Briefly, moderate grade was defined as patients with fever, respiratory symptoms and lung CT changed, but oxygen saturation exceeded 93% without oxygen; severe grade signifies respiratory frequency ≥ 30 times/minute, blood oxygen saturation ≤ 93%, oxygenation index ≤ 300 mmHg, and/or lung infiltration progression > 50% within 24 to 48 hours; and critical grade was defined as appearance of respiratory failure, septic shock, and/or multiple organ dysfunction or failure. Poor progression included moderate grade progressed to severe or critical grades and even death.

Statistical Analysis

SPSS software (version 22.0) was used to analyze the data. Shapiro wilktest method was used to determine the distribution of continuous variables. Student-t test was used to test the score difference of each group in the normal distribution, and rank sum test was used to compare the difference in the normal distribution. The normal distribution measurement data is expressed by mean ± standard deviation (SD), and median (interquartile Range IQR) for the non-normal distribution data. Frequency (percentage) was used to express the counting data. Chi-square test was used to compare the distribution differences among groups. When the number of predicted cases was less than 5, Fisher accurate probability method was applicated. The significant factors of univariable analysis were included into multivariable logistic regression model. A two-sided α of less than 0.05 was considered statistically significant.

Results

Demographic, clinical, and laboratory findings of COVID-19 patients

In this retrospective study, 528 patients diagnosed with COVID-19 were included, 41 patients with different tumor type (tumor group) and 487 patients without tumor (non-tumor group). Tumor type included 5 lung cancer, 5 gastrointestinal cancer, 5 blood cancer, 4 breast cancer, 4 head and neck cancer, 3 gynecological tumor, 3 liver cancer, 2 thyroid cancer, 2 urinary tumors, 2 prostate cancer, 2 esophagus cancer,1 pancreas cancer, 2 glioma and 1 osteosarcoma.

Compared with patients without tumor, patients with tumor were elder (median age 66 years [56-73] vs 58 years [39-68], p<0.001) (table 1). The gender distribution didn't show significant difference. As for the Laboratory findings, tumor group showed significant higher levels of white blood count (WBC), neutrophil count (NEUT), neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) than non-tumor group, but lymphocyte count (LY) and the level of serum albumin were lower in tumor group (table 1). The level of D-dimer in tumor group was elevated than non-tumor group, however, it did not showed any significance in the multivariable regression analyze (data not shown). Of the 35 (85.37%) moderate patients in tumor group, 18 (51.43%) experienced poor progression during subsequent hospitalization; while in non-tumor group, this proportion was 240 (54.42%) progression in 441 (90.55%) moderate patients. We observed no obvious difference in disease progression between two groups. In terms of mortality, our data still showed no significant difference (19.51% vs 11.91%, p=0.16, table 1).

Different characteristics of moderate and severe patients on admission

As in the early stage of COVID-19, most patients were mild or moderate, and the majority of mild patients were admitted to the Fangcang shelter hospitals. So almost all the patients admitted in our hospital during this period were moderate or severe cases. We explored the differences between moderate and severe patients at admission separately in patients with tumors and without tumors (table 2). In tumor group, severe patients showed marked lower LY (0.95[0.67-1.28] vs 0.45[0.37-0.82], p=0.014) and higher

NLR (4.51[2.16-7.23] vs 11.53 [11.34-13.30], p=0.031). Based on the results of univariable logistic regression, factors with p <0.05 were included for the multivariable logistic regression, only LY was negatively related to the severity (p=0.044). In non-tumor group, the levels of LY, NLR, D-dimer, CRP, and serum albumin were all significant different between moderate and severe patients. Then we did the multivariable regression and found only lower levels of LY and serum albumin were associated with the severity in COVID-19 patients without tumor.

Risk factors associated with poor progression among moderate patients

It was reported that almost 20% of COVID-19 patients with mild or moderate early presentation can develop severe or critical grade[13]. To further confirm the risk factors associated with poor progression among early moderate patients, we enrolled 476 moderate patients including 35 (7.35%) patients with tumor and 441 (92.65%) patients without tumor (table 1). According to the disease development, they were divided into two subgroups, stabilization and poor progression group (table 3). We found in patients with tumor, poor progression cases had higher CRP (5.19 [1.25-9.8] vs 1.47 [0.19-3.14], p=0.017) and lower serum albumin (32.0 [29.3-35.4] vs 37.7 [34.1-40.1], p=0.033) than stabilization patients, which also made sense in subsequent multivariable regression analysis (p=0.017 and p=0.033 separately). While in non-tumor moderate patients, older age, male, and higher levels of CRP were the risk factors associated with poor progression (table 3).

Risk factors associated with death in-hospital

We divided patients into survivor group and non-survivor group. The mortality was 19.51% in tumor group (table 1). The median age of non-survivors was 72 years old (IQR 71-80), elder than survivors (63, IQR 55-70) (p=0.006, table 4). But in multivariable logistic regression, this difference was meaningless; while higher NLR and CRP level were risk factors associated with death in-hospital among tumor patients (p=0.027 and 0.029 separately). In patients without tumor, older age, male, higher NLR and CRP were risk factors related to death in-hospital (table 4).

Discussion

In this retrospective study, we analyzed the data of 528 COVID-19 infected cases admitted in our hospital, which were divided into two groups, 41 patients accompanied with different tumors and 487 patients without tumor. The objective of this study was to compare the laboratory characteristics of these two groups and to explore risk factors for disease progression and survival separately.

Recent studies have indicated that lymphocyte count played a key role of severe or critical COVID-19 patients[14,15]. Lymphopenia is a common feature and thought to be a critical factor associated with disease severity and mortality[16]. In our study, we found severe patients were more likely accompanied by lymphopenia on admission, confirmed by univariable and multivariable logistic regression analyze, which is consistent with the results of Qin et al[17]. Absolute counts of lymphocytes on admission were lower in severe patients when compared to moderate patients both in tumor group and non-tumor group. We

found lymphopenia was valuable in determination the severity of COVID-19 patients. Besides, lymphocytes count was significant lower in tumor group related to non-tumor group.

The NLR in peripheral blood was a well-known marker of systemic inflammatory responses. Even though the underlying mechanisms are not fully known, it has been confirmed that circulating neutrophil counts were elevated above the normal range in tumor patients[18]. Elevated NLR has been observed in multiple solid cancers, including pancreas cancer[19], non-small cell lung cancer[20], cervical adenocarcinoma[21], glioma[22], and thought to be related to poorer survival, as well as to predict tumor grade[23] and distinguish between tumor recurrence and pseudoprogression in high-grade gliomas[24].

As it has been reported that the increase of NLR was associated with more serious infections[17,25], and identified as an independent risk factor for COVID-19 patients with severe illness[26]. Our results confirmed the increase of NLR was positively correlated with the poor outcome both in tumor and non-tumor group by multivariable logistic regression analysis. In general, the NLR in tumor group was significantly elevated in contrast to the other group.

Kaya et al. reported the inflammatory cytokines secreted by tumor cells caused the neutrophil count to increase, both in tumor stroma and in peripheral blood. The increase in the neutrophil count may cause a decrease in lymphocytes and lymphocyte apoptosis, as a result cellular immunity is depressed[27]. This interaction between neutrophils and lymphocytes probably explained the increased neutrophil and NLR level with decreased lymphocyte count in tumor group.

Serum albumin is an indicator of nutritional status, and hypoalbuminemia reflects undernourished state in the elderly, patients with chronic diseases and cancer[28]. In patients with inflammatory conditions, serum albumin levels were significantly reduced and negatively correlated with disease severity[29]. We showed coherent result in non-tumor group by univariable and multivariable logistic regression analyze. Tumor patients are frequently combined with cachexia in various degrees according to tumor type and stage[30]. One of the most characteristic biochemical indicators of cachexia is hypoalbuminemia. It has been reported that patient with serum-albumin < 35 g/L was associated with reduced quality of life and immune function, while serum-albumin < 32 g/L with shorter survival[29,31]. Logically, we found reduced serum albumin in tumor group in our study, and albumin level was negatively related to inflammatory progression in COVID-19 patients with tumor.

Serum CRP, a sensitive and acute-phase protein synthesized by hepatocytes following stimulation by various cytokines, including tumor necrosis factor-α and interleukin (IL)-6, markedly increase within several hours of infection or inflammation. CRP ≥ 5 mg/dl was considered as an important evidence of severe inflammation. Elder patients with higher CRP had higher in-hospital mortality with a RR of 2 compared with lower CRP group[32]. Furthermore, CRP level is regarded as a useful marker of systemic inflammation and a key feature of cancer cachexia. CRP > 1 mg/dl was associated with reduced immune function and shorter survival in tumor patient[31]. The production of CRP was elevated in tumor patients

with cachexia[30]. Similarly in our results, CRP was positively associated with poor progression and death in both tumor and non-tumor group. CRP level of non-survivors and progression cases in tumor group was superior to 5 mg/dl (median of 10.44 and 5.19 separately). It's worth mentioning that tumor cells could also affect the production of CRP, which caused more incidence of hyper inflammation. Studies showed that pro-inflammatory cytokines are produced not only by inflammatory cells, but also by tumor cells. Among which, IL-6 was widely involved[33]. In consequence, CRP level in tumor patients was logically elevated.

Our data represented that COVID-19 patients with tumor showed elevated NLR, CRP levels and more severe lymphopenia and hypoalbuminemia compared with patients without tumor. All these biochemical indicators signified higher probability of infection progression possibility and mortality. Actually in our study, we showed discordant results: we observed the tendency of increased mortality in tumor group (19.5% vs 11.9%), but was not statistically significant. Meanwhile, the severity grading and progression rate was similar in COVID-19 patients with and without tumors. One explanation might be that patients with cancer could experience systemic immunosuppressive states caused by both cancer and anticancer treatments[34]. Studies have shown that development of cancer is frequently associated with inhibited immune status initiated by certain factors that inhibit effector T cell functions (TGF-β, IL-10, VEGF…) and recruit regulatory cells to generate an immunosuppressive microenvironment (IL-4, GM-CSF, IL-1β, VEGF…)[35,36]. The interaction between systemic inflammation and tumor immunosuppressive state demands further investigation.

Conclusion

Our analyze showed the disease severity at hospitalization, progression rate and mortality were equal between tumor and non-tumor group. As one of combined diseases, malignancy history may have no marked effect on the severity and prognosis of COVID-19. Nevertheless, leucocyte count, neutrophil count, NLR, CRP and D-dimer levels were elevated in COVID-19 patients with cancer, with lower level of lymphocyte count and albumin. Lymphopenia was negatively related to the determination of severity at hospitalization both in patients with and without tumor; NLR was positively correlated with the poor outcome in either group. CRP was relevant to the disease progression and survival. ALB was related to disease progression in tumor group, and severity in non-tumor group.

There were some limitations in this study. First, due to the rapid pandemic outbreak and the shortage of medical workers, not all historical electronic medical records of patients were completely connected, thus a main limitation was the self-report of medical history by patients on admission. The clinical staging and precise treatment protocols were imprecise or even unavailable. We could not conclude the effect of forepassed application of radiotherapy (especially in lung cancer) or chemotherapy agent to the progression the COVID-19. Secondly, the time from onset to progression couldn’t be analyzed as a risk factor because of the incomplete data about the length of time before hospital admission. Besides, due to the retrospective study design, not all laboratory tests were performed in each patient, immunological indicators as IL-6, IL-17A, CD4 + T cell, and CD8 + T cell in particular. Therefore, profound immunological

alterations were not concluded. Moreover, our study was single-central and small-sized with biased patient characteristics, these may make it difficult to generalize the result, larger sample population of multiple centers will be more representative.

Abbreviations

COVID-19
coronavirus disease 2019
SARS-CoV-2
severe acute respiratory syndrome coronavirus 2
COPD
chronic obstructive pulmonary disease
NHC
National Health Commission
IQR
inter quartile range
SD
standard deviation
WBC
white blood cell count
NEUT
neutrophil count
LY
lymphocyte count
NLR
neutrophil-to-lymphocyte ratio
CRP
C-reactive protein
ALB
serum albumin
IL-6
interleukin-6

Declarations

Ethics approval and consent to participate

The study was approved by The Central Hospital of Wuhan Hospital Ethics Committee and written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases (No. 2020-183).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

There was no funding for the study.

Authors' contributions

Drs Jiahao Hu and Haixia Ding contributed equally as co-first authors.

Concept and design: Haixia Ding, Jiahao Hu, Xiaowu Shi

Acquisition, analysis, or interpretation of data: Jiahao Hu, Shenglan Ye, Xiuwen Yang,

Drafting of the manuscript: Haixia Ding, Jiahao Hu

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Supervision: Xiaowu Shi

Acknowledgement

We acknowledge all health-care workers involved in the diagnosis and treatment of patients with COVID-19 in Hubei Province, especially medical support teams from all over China.

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Tables

Table 1: Demographic, laboratory findings, and outcomes of COVID-19 patients.

	Tumor (n=41)	Non-tumor (n=487)	*P* value
Age, median (IQR), years	66 (56-73)	58 (39-68)	0.001
Gender			
Female (%)	21 (51.22)	264 (54.21)	0.71
Male (%)	20 (48.78)	223 (45.79)	
Laboratory findings			
WBC, median (IQR), $\times 10^9$/L	5.89 (4.07-7.53)	5.07 (3.91-6.54)	0.044
NEUT, median (IQR), $\times 10^9$/L	4.28 (2.36-6.42)	3.20 (2.39-4.55)	0.012
LY, median (IQR), $\times 10^9$/L	0.88 (0.58-1.24)	1.16 (0.83-1.56)	0.001
NLR, median (IQR)	5.09(2.69-9.25)	2.70 (1.73-4.92)	< 0.001
CRP, median (IQR), mg/dl	3.05 (0.44-7.73)	0.92 (0.14-3.84)	0.003
ALB, median (IQR), g/L	35.2 (31.5-37.7)	39.1 (35.5-42.6)	< 0.001
Severity			
Severe (%)	6 (14.6)	46 (9.45)	0.28
Moderate (%)	35 (85.37)	441 (90.55)	
Progression among moderate patients			
Stabilization (%)	17 (48.57)	201 (45.58)	0.73
Poor progression (%)	18 (51.43)	240 (54.42)	
Outcomes			
Survivor (%)	33 (80.49)	429 (88.09)	0.16
Non-survivor (%)	8 (19.51)	58 (11.91)	

WBC = white blood cell count; NEUT = neutrophil count; LY = lymphocyte count; NLR = neutrophil-to-lymphocyte ratio; CRP = C-reactive protein; ALB = Serum albumin

Table 2: Different characteristics of moderate and severe patients on admission.

Tumor patients	Moderate (n=35)	Severe (n=6)	*P* value	Multivariable (95% CI for OR)	*P* value
Age, median (IQR), years	65.5 (57-74)	66 (53-72)	0.577		
Gender					
Female (%)	16 (45.71)	4 (66.67)	0.41		
Male (%)	19 (54.29)	2 (33.33)			
Laboratory findings					
WBC, median (IQR), $\times 10^9$/L	5.89 (4.13-7.51)	6.29 (3.67-7.54)	>0.999		
NEUT, median (IQR), $\times 10^9$/L	4.09 (2.24-6.27)	4.79 (3.10-6.58)	0.552		
LY, median (IQR), $\times 10^9$/L	0.95 (0.67-1.28)	0.45 (0.37-0.82)	0.014	0.019 (0-0.094)	0.044
NLR, median (IQR)	4.51 (2.16-7.23)	11.53 (11.34-13.30)	0.031	1.03 (0.863-1.23)	0.743
CRP, median (IQR), mg/dl	2.97 (0.39-6.19)	6.09 (2.10-9.31)	0.24		
ALB, median (IQR), g/L	34.8 (30.6-37.8)	35.55 (33.2-36.7)	0.957		
Non-tumor patients	**Moderate (n=441)**	**Severe (n=46)**	***P* value**	**Multivariable (95% CI for OR)**	***P* value**
Age, median (IQR), years	58 (38-68)	62 (55-69)	0.05		
Gender					
Female (%)	200 (45.71)	23 (50)	0.547		
Male (%)	241 (54.29)	23 (50)			
Laboratory findings					
WBC, median (IQR), $\times 10^9$/L	5.11 (3.96-6.67)	4.76 (3.60-6.06)	0.084		
NEUT, median (IQR), $\times 10^9$/L	3.19 (2.36-4.54)	3.34 (2.53-4.58)	0.427		
LY, median (IQR), $\times 10^9$/L	1.21	0.70 (0.52-1.01)	<0.001	0.168 (0.061-0.462)	0.001

	(0.88-1.63)				
NLR, median (IQR)	2.59 (1.67-4.90)	5.00 (2.86-9.88)	<0.001	0.962 (0.889-1.04)	0.33
CRP, median (IQR), mg/dl	0.67 (0.12-3.19)	4.61 (2.94-6.47)	<0.001	1.08 (0.991-1.177)	0.08
ALB, median (IQR), g/L	39.6 (35.2-42.9)	33.5 (31.2-37.6)	<0.001	0.847 (0.782-0.918)	<0.001

WBC = white blood cell count; NEUT = neutrophil count; LY = lymphocyte count; NLR = neutrophil-to-lymphocyte ratio; CRP = C-reactive protein; ALB = Serum albumin.

Table 3: Risk factors associated with poor progression among moderate patients.

Tumor patients	Stabilization (n=17)	Poor progression (n=18)	*P* value	Multivariable (95% CI for OR)	*P* value
Age, median (IQR), years	62 (55-69)	70 (62-85)	0.074		
Gender					
Female (%)	8 (47.06)	11 (61.11)	0.505		
Male (%)	9 (52.94)	7 (38.89)			
Laboratory findings					
WBC, median (IQR), $\times 10^9$/L	5.80 (3.58-7.51)	5.90 (4.34-7.51)	0.463		
NEUT, median (IQR), $\times 10^9$/L	4.09 (2.12-6.22)	4.47 (2.38-6.27)	0.382		
LY, median (IQR), $\times 10^9$/L	0.96 (0.62-1.22)	0.85 (0.68-1.4)	0.804		
NLR, median (IQR)	4.23 (2.16-7.24)	5.24 (3.20-7.24)	0.458		
CRP, median (IQR), mg/dl	1.47 (0.19-3.14)	5.19 (1.25-9.82)	0.011	1.334 (1.052-1.690)	0.017
ALB, median (IQR), g/L	37.7 (34.1-40.1)	32.0 (29.3-35.4)	0.003	0.804 (0.658-0.983)	0.033
Non-tumor patients	**Stabilization (n=201)**	**Poor Progression (n=240)**	***P* value**	**Multivariable (95% CI for OR)**	***P* value**
Age, median (IQR), years	47 (33-65)	62 (47-70)	<0.001	1.023 (1.010-1.037)	0.001
Gender					
Female (%)	133 (66.17)	108 (45)	<0.001	0.509 (0.326-0.794)	0.003
Male (%)	68 (33.83)	132 (55)			
Laboratory findings					
WBC, median (IQR), $\times 10^9$/L	5.18 (4.05-6.25)	4.96 (3.90-6.76)	0.864		
NEUT, median (IQR),	3.03 (2.24-	3.26 (2.38-	0.053		

$\times 10^9$/L	4.24)	6.27)			
LY, median (IQR), $\times 10^9$/L	1.40 (1.05-1.86)	1.03 (0.73-1.40)	<0.001	0.826 (0.616-1.108)	0.202
NLR, median (IQR)	2.00 (1.44-3.13)	3.30 (2.06-5.40)	<0.001	1.056 (0.961-1.161)	0.258
CRP, median (IQR), mg/dl	0.28 (0.06-1.00)	2.03 (0.34-4.73)	<0.001	1.303 (1.157-1.467)	0.003
ALB, median (IQR), g/L	40.6 (37.5-43.4)	38.6 (34.9-41.7)	<0.001	0.987 (0.935-1.042)	0.633

WBC = white blood cell count; NEUT = neutrophil count; LY = lymphocyte count; NLR = neutrophil-to-lymphocyte ratio; CRP = C-reactive protein; ALB = Serum albumin.

Table 4: Risk factors associated with death in-hospital.

Tumor patients	Survivor (n=33)	Non-survivor (n=8)	*P* value	Multivariable (95% CI for OR)	*P* value
Age, median (IQR), years	63 (55-70)	72 (71-80)	0.006	1.936 (0.814-4.606)	0.135
Gender					
Female (%)	19 (57.58)	6 (75)	0.13		
Male (%)	14 (42.42)	2 (25)			
Laboratory findings					
WBC, median (IQR), $\times10^9$/L	5.90 (4.34-7.51)	5.31 (3.53-9.82)	0.742		
NEUT, median (IQR), $\times10^9$/L	4.09 (2.33-6.22)	4.92 (3.53-8.24)	0.107		
LY, median (IQR), $\times10^9$/L	0.96 (0.68-1.26)	0.54 (0.39-0.67)	0.01	0.042 (0.001-5.772)	0.207
NLR, median (IQR)	4.46 (2.16-7.24)	11.61 (0.94-12.46)	0.004	1.371 (1.037-1.813)	0.027
CRP, median (IQR), mg/dl	2.17 (0.39-4.54)	10.44 (8.74-12.18)	0.003	1.344 (1.075-1.679)	0.009
ALB, median (IQR), g/L	36.7 (32.0-37.8)	31.7 (28.5-35.2)	0.029	0.430(0.128-1.450)	0.174
Non tumor patients	**Survivor (n=429)**	**Non-survivor (n=58)**	***P* value**	**Multivariable (95% CI for OR)**	***P* value**
Age, median (IQR), years	57 (37-67)	69 (58-83)	<0.001	1.062 (1.035-1.090)	<0.001
Gender					
Female (%)	245 (47.06)	19 (61.11)	<0.001	0.939 (0.868-1.016)	0.022
Male (%)	184 (52.94)	39 (38.89)			
Laboratory findings					
WBC, median (IQR), $\times10^9$/L	5.01 (3.94-6.28)	5.86 (3.70-7.72)	0.13		
NEUT, median (IQR), $\times10^9$/L	3.16 (2.39-4.39)	4.12 (3.40-6.50)	0.018	0.829 (0.670-1.004)	0.055

LY, median (IQR), $\times 10^9$/L	1.21 (0.89-1.62)	0.65 (0.47-1.02)	<0.001	1.204 (0.896-1.617)	0.218
NLR, median (IQR)	2.51 (1.65-4.53)	4.89 (3.19-10.68)	<0.001	1.155 (1.057-1.262)	0.001
CRP, median (IQR), mg/dl	0.65 (0.12-3.04)	4.72 (2.66-8.09)	<0.001	1.183 (1.093-1.281)	<0.001
ALB, median (IQR), g/L	39.6 (36.2-42.9)	34.6 (32.7-39.1)	<0.001	0.939 (0.868-1.016)	0.116

WBC = white blood cell count; NEUT = neutrophil count; LY = lymphocyte count; NLR = neutrophil-to-lymphocyte ratio; CRP = C-reactive protein; ALB = Serum albumin