

High number and specific comorbidities independently of age are closely related to progression and poor prognosis in patients with COVID-19

Dafeng Liu (✉ ldf312@126.com)

the Public and Health Clinic Center of Chengdu <https://orcid.org/0000-0002-6792-641X>

Yongli Zheng

the Public and Health Clinic Center of Chengdu

Jun Kang

the Public and Health Clinic Center of Chengdu

Dongmei Wang

the Public and Health Clinic Center of Chengdu

Lang Bai

Sichuan University West China Hospital

Yi Mao

the Public and Health Clinic Center of Chengdu

Guifang Zha

the Public and Health Clinic Center of Chengdu

Hong Tang

Sichuan University West China Hospital

Rengqing Zhang

the Public and Health Clinic Center of Chengdu

Research

Keywords: coronavirus disease 2019 (COVID-19), comorbidity, number, progression, prognosis

Posted Date: June 29th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-576949/v2>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background— Some patients with comorbidities and rapid disease progression have a poor prognosis.

Aim—In this study, we aimed to investigate the distribution characteristics of comorbidities and their relationship with disease progression and outcomes of COVID-19 patients.

Methods— A total of 718 COVID-19 patients were divided into five clinical type groups and eight age-interval groups. The distribution characteristics of comorbidities were compared between the different clinical type groups and between the different age-interval groups, and their relationships with disease progression and outcomes of COVID-19 patients were assessed.

Results—Approximately 88.62% (637/718) of the COVID-19 patients were twenty to fifty-nine years old. Approximately 65.73% (554/718) had one or more comorbidities, and common comorbidities included non-alcoholic fatty liver disease (NAFLD), hyperlipidaemia, hypertension, diabetes mellitus (DM), chronic hepatitis B (CHB), hyperuricaemia and gout. COVID-19 patients with comorbidities were older, especially those with chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD). Hypertension, DM, COPD, chronic kidney disease (CKD) and CVD were mainly found in severe COVID-19 patients. According to spearman and partial correlation analysis the number of comorbidities was correlated positively with disease severity, the number of comorbidities and NAFLD were correlated positively with virus negative conversion time, hypertension, CKD and CVD were primarily associated with those who died, and the above-mentioned correlation existed independently of age. Risk factors included the number of comorbidities and hyperlipidaemia for disease severity, age, the number of comorbidities, hyperlipidaemia, NAFLD and COPD for the virus negative conversion time, and the number of comorbidities and CKD for prognosis. Number of comorbidities played a predictive role in disease progression and outcomes.

Conclusions—High number and specific comorbidities independently of age are closely related to progression and poor prognosis in patients with COVID-19. These findings provide a reference for clinicians to focus on the number and specific comorbidities in COVID-19 patients to predict disease progression and prognosis.

Clinical Trial Registry: Chinese Clinical Trial Register ChiCTR2000034563

A statement about the manuscript in research square

This manuscript has been presented as preprint in the research square according to the following link:

<https://www.researchsquare.com/article/rs-576949/v2>.

Introduction

The worldwide pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, namely, coronavirus disease 2019 (COVID-19) presents a paramount and urgent threat to global health. [1-5] As of May 11, 2021, there were approximately 157,362,408 confirmed cases, including 3,277,834 deaths, reported worldwide. [6] Although the overall prognosis of COVID-19 is good, [1-5] some patients with comorbidities or rapid disease progression have a poor outcome. [7-12]

Previous studies have shown that approximately 66.67~70.70% of COVID-19 patients have comorbidities; common comorbidities are hypertension, cardiovascular disease (CVD), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), malignancy, chronic kidney disease (CKD), and obesity. [13-15] DM, hypertension, CVD, active malignancy, and a high number of comorbidities are risk factors for a worse outcome. [16-19] DM and hypertension, or CVD are common underlying diseases related to death in hospitalized cases. [14]

The distribution characteristics of comorbidities in different age intervals and clinical types and whether other comorbidities are also related with the progression and prognosis of COVID-19 are unknown and worth studying.

Methods

2.1 Subjects

This study had a [cross-sectional](#) research design.

In total, 718 COVID-19 patients from the hospital isolation ward who presented to the Public and Health Clinic Centre of Chengdu from January 16, 2020, to April 30, 2021, were retrospectively recruited (Figure 1). The Ethics Committee of the Public and Health Clinic Centre of Chengdu approved this study (ethics approval number: PJ-K2020-26-01). Written informed consent was waived by the Ethics Commission of the designated hospital because this study was related to emerging infectious diseases.

2.2 Clinical typing, disease diagnosis and cure criteria

The criteria for COVID-19 clinical typing and disease diagnosis were based on the seventh Trial Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Guidance. [7]

2.3 Grouping standards

Seven hundred eighteen COVID-19 patients were enrolled (Figure 1), including 681 and 37 non-severe (asymptomatic infection, light and common) and severe (severe and critical illness) cases, respectively (Table 1, Figure 1). Of these patients, 710 and 8 cases were divided into a survival subgroup (those who survived) and a death subgroup (those who died), respectively (Table 1, Figure 1).

Based on every 10 years as an age interval, 12, 16, 182, 204, 157, 94, 34 and 21 cases were divided into eight age-interval subgroups of 0~9, 10~19, 20~29, 30~39, 40~49, 50~59, 60~69, >70 years, respectively (Figure 2A).

Based on the type of comorbidity, 82, 133, 47, 195, 63, 59, 15, 10, 11, 18 and 34 cases were divided into a hypertension subgroup (those with hypertension), hyperlipidaemia subgroup (those with hyperlipidaemia), hyperuricaemia and gout subgroup (those with hyperuricaemia and gout), non-alcoholic fatty liver disease (NAFLD) subgroup (those with NAFLD), DM subgroup (those with DM), chronic hepatitis B (CHB) subgroup (those with CHB), COPD subgroup (those with COPD), CKD subgroup (those with CKD), CVD subgroup (those

with CVD), cancer abovementioned subgroup (those with cancer), and other comorbidity subgroup (those with abovementioned comorbidity) (Figure 2B), respectively.

The 718 COVID-19 patients were also divided according to the number of comorbidities into a no comorbidity subgroup (patients without comorbidities), one comorbidity subgroup (patients with one comorbidity), two comorbidity subgroup (patients with two comorbidities), and three and more comorbidity subgroup (patients with three and more comorbidities), with 253,193,127 and 145 cases, respectively (Figure 4A).

According to clinical type, 234, 73, 371, 18 and 19 cases were divided into an asymptomatic infection group (patients belonging to symptom infection clinical type), a light group (patients belonging to light clinical type), a common group (patients belonging to common clinical type), a severe group (patients belonging to severe clinical type), and a critically ill group (patients belonging to critically illness clinical type), respectively (Figure 4B).

2.4 Data collection

Demographic data, clinical data, and lymphocyte and subset counts for all 718 cases were collected and used to establish databases. The authenticity, accuracy and completeness of the data were strictly controlled.

2.5 Statistical analysis

Statistical analyses were performed using GraphPad Prism 8 (GraphPad, CA, USA) and SPSS 26.0 (SPSS, Chicago, IL, USA). Measurement data are expressed as $x \pm SD$, and ANOVA was used for multigroup comparisons of the homogeneity of variance and normally distributed data. A least significant difference (LSD) t-test was used for further comparisons between two groups. An independent-sample t-test was employed for comparisons between two groups. A percentage or proportion was used to express enumeration data, and a chi-square test and Fisher's exact test were applied for comparisons of these data. Spearman correlation analysis and partial correlation analysis were used for two-factor correlation analysis. Receiver operating characteristic (ROC) analysis for age was performed to assess the ability to distinguish between non-severe and severe patients and between surviving patients and those who died. Statistical significance was defined as $P < 0.05$.

Results

3.1 General conditions

Approximately 5.16% (37/718) (Table 1, Figure 5A) of patients had severe COVID-19, and 1.11% (8/718) (Table 1, Figure 5B) of severe COVID-19 patients died.

For the distribution characteristics of age, approximately 88.62% (637/718) (Figure 2A) of COVID-19 patients were twenty to fifty-nine years old. A small number of patients were younger than 20 years old or older than 60 years old (Figure 2A).

Patients in each comorbidity subgroup were older than those in the no-comorbidity subgroup (Figure 3), especially those with COPD and CVD (Figure 3). Except for the CKD subgroup and the cancer subgroup, the differences were statistically significant (all $P \leq 0.001$).

In this COVID-19 cohort, the order of clinical type according to the number of cases was as follows: common, asymptomatic infection, light, critical illness and severe. The percentages were 51.67%, 32.59%, 10.17%, 2.65%, and 2.51%, respectively (Figure 4B).

Severe cases (critical illness and severe clinical type) were distributed in age-interval subgroups older than twenty years, especially in the subgroup of patients older than seventy years (Figure 5A). Those who died were in the older than sixty age-interval subgroup, especially in those older than seventy (Figure 5B).

3.2 The distribution characteristics of comorbidities in different clinical type groups and different age-interval subgroups

Approximately 65.73% (554/718) (Figure 4A) of COVID-19 patients had one or more comorbidities, and 37.85% (176/718) of patients had two or more comorbidities.

Common comorbidities were NAFLD, hyperlipidaemia, hypertension, DM, CHB, hyperuricaemia and gout (Figure 2B). Cancer, COPD, CVD, CKD and other comorbidities were rare (Figure 2B).

Among COVID-19 patients, hypertension, DM, COPD and CVD were mainly found in patients with the critically ill clinical type (Figure 6A, 6E, 6G, 6I), CKD and CVD were mainly found in patients with the common and severe clinical type (Figure 6H, 6I), and hyperuricaemia and gout (Figure 6B) were mainly found in patients with the common clinical type. NAFLD (Figure 6D) was rare in those with the severe clinical type.

Among COVID-19 patients, hypertension, CHB, COPD and CVD (Figure 7A, 7F, 7G, 7I) were mostly distributed in those aged 50 and 80 years old. Cancer, CKD and other comorbidities (Figure 7H, 7J, 7K) mostly occurred in patients older than 70 years. DM, hyperlipidaemia, hyperuricaemia and gout, and NAFLD (Figure 7B, 7C, 7D, 7E) were mostly distributed in patients aged 20 and 70 years.

3.3 The relationship of comorbidities with disease progression and prognosis in COVID-19 patients

In the severe group, patients were older than those in the non-severe group and had a greater number of comorbidities (Table 2) (all $P < 0.0001$). However, there were no differences in comorbidities between the two groups (Table 2) ($P \geq 0.05$).

In the non-surviving group, patients were older than those in the surviving group and had a greater number of comorbidities, more hypertension, more chronic kidney disease and more cardiovascular diseases (Table 3) (all $P < 0.05$). No differences in other comorbidities between the two groups were detected (Table 3) ($P \geq 0.05$).

According to Spearman correlation analysis, only the number of comorbidities was correlated positively with disease severity (Table 4), though no specific comorbidity correlated with disease severity (Table 4). Moreover, the number of comorbidities, NAFLD, CHB and COPD were all correlated positively with virus negative

conversion time (Table 4), and the number of comorbidities, CKD, CVD and hypertension correlated positively with prognosis (Table 4). While when the age was controlled, according to partial correlation analysis, the number of comorbidities was also correlated positively with disease severity (Table 5), the number of comorbidities and NAFLD were also correlated positively with virus negative conversion time (Table 5), and CKD, CVD and hypertension correlated positively with prognosis (Table 5). But there was no longer any correlation between CHB, COPD and virus negative conversion time, and between the number of comorbidities and prognosis (Table 5).

According to multiple stepwise regression analysis for disease severity, risk factors included the number of comorbidities and hyperlipidaemia (Table 6). Risk factors for virus negative conversion time were the number of comorbidities, hyperlipidaemia, NAFLD and COPD (Table 6). Furthermore, risk factors for prognosis were the number of comorbidities and CKD (Table 6).

3.4 The prediction of number of comorbidities on disease progression and the outcomes of COVID-19 patients

According to the ROC analysis, number of comorbidities could predict disease progression and patient outcomes (Table 7, 8). The best cutoff point for distinguishing the severe cases from the non-severe cases was more than three comorbidities (Table 7). Its area under the curve was 0.864, (Table 7, Figure 8). Its sensitivity was 75.70% (Table 7). Its specificity was 88.00% (Table 7). The best cutoff point for distinguishing the dead cases from the survival cases was more than four comorbidities (Table 8). Its area under the curve was 0.947, (Table 8, Figure 9). Its sensitivity was 85.70% (Table 8). Its specificity was 91.60% (Table 8).

Discussion

In this COVID-19 cohort, the prevalence of severity was 5.16%, and mortality was 1.11%. Most patients with severe disease were older than thirty years, especially older than seventy, and most deaths occurred in those older than seventy years. Overall, age correlated with severity. This finding is consistent with the literature that old age is associated with the progression of COVID-19 and is an independent risk factor for progression [20] and that advanced age is a risk factor for a worse outcome in association with higher death rates. [16-19]

Approximately 65.73% of the patients in this COVID-19 cohort had one or more comorbidities, and 37.85% had two or more. This is consistent with a report that one-third of patients have no comorbidity according to medical records,[14] but it is lower than the report that 70.7% of patients have one chronic condition and higher than the report that 20.9% patients have 2 or more. [15] Further analysis found that severe cases had more comorbidities than non-severe cases; those who died had more comorbidities than surviving patients. An increased number of comorbidities correlated positively with disease severity and poor prognosis and was also an independent risk factor for progression and poor prognosis. This was consistent with previous findings that the number of comorbidities is a risk factor for a worse outcome [16-18,21]

In this study, common comorbidities were mainly NAFLD, hyperlipidaemia, hypertension, DM, CHB, hyperuricaemia and gout; cancer, COPD, CVD, CKD and other comorbidities were not common. We found more types of comorbidities, especially metabolic diseases such as NAFLD, hyperlipidaemia, hyperuricaemia and gout in this COVID-19 cohort. The findings are not completely consistent with the report of common

comorbidities in hospitalized patients of hypertension, CVD, DM, asthma, COPD, and other underlying diseases,[14] or the systematic review and meta-analysis of 76993 patients that hypertension, CVD, DM, smoking, COPD, malignancy, and CKD, were most prevalent among patients with COVID-19. [13]

Moreover, hypertension, DM, COPD, CKD and CVD were mainly present in patients with severe disease who were older than fifty years, especially among those seventy years old. Hypertension, CKD and CVD were common in patients who died and were older than seventy years. The number of comorbidities was correlated positively with disease severity, the number of comorbidities and NAFLD were correlated positively with virus negative conversion time, hypertension, CKD and CVD were primarily associated with those who died, and the above-mentioned correlation existed independently of age. These findings were not completely consistent with the literature report that DM and HBP or CVD are common underlying diseases related to death in hospitalized cases, [14] that COPD increases the risks of death and negative outcomes in patients with severe COVID-19,[22] that impaired renal function is an independent predictor of in-hospital death, [23] and that risk of death is associated with pre-existing hypertension, diabetes, or chronic kidney disease. [21]

In this study we found that number of comorbidities played a predictive role in distinguishing severe cases from nonsevere patients and in distinguishing dead cases from surviving cases. More than three and more than four comorbidities predict disease progression, a poor prognosis, respectively.

Based on these findings, independently of age, three or more comorbidities, and some specific comorbidities, such as hypertension, CKD and CVD, are related to progression and death in hospitalized COVID-19 patients.

Our study had several limitations. First, it was a retrospective, single-centre study. Second, the number of severe cases, particularly deaths, was small. Despite these limitations, we report several novel findings: in addition to the common comorbidities reported in the literature, more types of comorbidities, especially metabolic diseases such as NAFLD, hyperlipidaemia and hyperuricaemia, were present in this COVID-19 cohort. Independently of age, two or more comorbidities, and some specific comorbidities, such as hypertension, CKD and CVD, are related to progression and death in hospitalized COVID-19 patients.

Conclusions

In addition to the common comorbidities reported in the literature, there were more types of comorbidities, especially metabolic diseases such as NAFLD, hyperlipidaemia and hyperuricaemia, in this COVID-19 cohort. Independently of age, two or more comorbidities, and some specific comorbidities, such as hypertension, CKD and CVD, are related to progression and death in hospitalized COVID-19 patients. These findings provide a reference for clinicians to focus on the number and specific comorbidities in COVID-19 patients to predict disease progression and prognosis.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the Public and Health Clinic Centre of Chengdu approved this study (ethic approval number: PJ-K2020-26-01). Written informed consent was waived by the Ethics Commission of the designated

hospital because this study is related to emerging infectious diseases.

Consent for publication

All of participants understand that the information will be published without their child or ward's/their relative's (circle as appropriate) name attached, but that full anonymity cannot be guaranteed. All of participants understand that the text and any pictures or videos published in the article will be freely available on the internet and may be seen by the general public. The pictures, videos and text may also appear on other websites or in print, may be translated into other languages or used for commercial purposes. All of participants have been offered the opportunity to read the manuscript.

Availability of data and materials

All data, models, or code generated or used during the study are available from the first author by request: Dafeng Liu, E-mail: liudf312@126.com

Competing interests

The authors declare that they have no competing interests.

Funding

This research was supported by the Thirteenth Five-Year Project on Tackling Key Problems of National Science and Technology (2017ZX10305501008), the Nonprofit Central Research Institute Fund of the Chinese Academy of Medical Sciences (2020-PT330-005), the Sichuan Science and Technology Program (2020YFS0564), The Chengdu Municipal Science and Technology Bureau Science and Technology Huimin Major Demonstration Project (00092), the Sichuan Province Health Commission (17PJ070), the Chengdu Municipal Health Commission (2019079), and the Chengdu Science and Technology Bureau (2020-YF05-00191-SN).

Authors' contributions

Concept and design: Dafeng Liu, Yongli Zheng, Jun Kang, Dongmei Wang, Yi Mao, Guifang Zha, Hong Tang, Rengqi Zhang and Lang Bai; Data acquisition: Dafeng Liu, Yongli Zheng, Jun Kang, Dongmei Wang, Yi Mao, Guifang Zha; data analysis and interpretation: Dafeng Liu, Yongli Zheng, Jun Kang, Dongmei Wang, Yi Mao, Guifang Zha; Drafting the manuscript: Yongli Zheng, Jun Kang, Dongmei Wang; administrative, technical, or material support: Yongli Zheng, Jun Kang, Dongmei Wang, Hong Tang and Lang Bai; study supervision: Hong Tang, Rengqi Zhang and Lang Bai.

ORCID

Dafeng Liu^{1D}<https://orcid.org/0000-0002-6792-641X>

Acknowledgements

Thanks to Dr. Xiu Li and Yaling Liu (the Public and Health Clinic Centre of Chengdu, rehabilitation division).

References

1. Wu G, Gao GF, Tan W, *et al.* A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* **2020**;382(8):727-733.
2. Lu H, Stratton CW, Tang YW. Outbreak of Pneumonia of Unknown Etiology in Wuhan China: the Mystery and the Miracle. *J Med Virol.* **2020**;92(4):401-402.
3. Ji W, Wang W, Zhao X, *et al.* Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J Med Virol.* **2020**;92(4): 433-440.
4. Gates B. Responding to COVID-19- A Once-in-a-Century Pandemic? *N Engl J Med.* **2020**; 382(18):1677-1679.
5. Wu F, Zhao S, Yu B, *et al.* A new coronavirus associated with human respiratory disease in China. *Nature.* **2020**; 579:265–9.
6. World Health Organization, Weekly epidemiological update on COVID-19 - 11 May 2021. Available online: [https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19--11-may-2021/\(accessed on 11 May 2021\).](https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19--11-may-2021/(accessed%20on%2011%20May%202021).)]
7. National Health Commission of the People's Republic of China. The seventh Trial Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Guidance. Available at:<http://medjournals.cn/2019NCP/index.do;jsessionid=F12B0B0FEBD6E6193A01B01FEA4E8109>] [External Link]
8. Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* **2020**;395(10223):497-506.
9. Chen N, Zhou M, Dong X, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* **2020**;395(10223):507-513.
10. Wang D, Hu B, Hu C, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* **2020**; 323(11):1061-1069.
11. Guan WJ, Ni ZY, Hu Y, *et al.* Clinical Characteristics of 2019 Novel Coronavirus Infection in China. *N Engl J Med.* **2020**; 382(18):1708-1720.
12. Wilson N, Kvalsvig A, Barnard LT, *et al.* Case-Fatality Risk Estimates for COVID-19 Calculated by Using a Lag Time for Fatality. *Emerg Infect Dis.* **2020**;26(6):1339-1441.
13. Emami A, Javanmardi F, Pirbonyeh N, *et al.* Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. *Arch Acad Emerg Med.* **2020**;8(1): e35.
14. Mostafaei A, Ghojzadeh M, Hajebrahimi S, *et al.* Clinical Presentation of Iranian Patients Affected with COVID-19: A Thousand Faces Disease. *Iran J Allergy Asthma Immunol.* **2021**; 20(2):140-146.
15. Alqahtani AM, AlMalki ZS, Alalweet RM, *et al.* Assessing the severity of illness in patients with coronavirus disease in Saudi Arabia: a retrospective descriptive cross-sectional study. *Front Public Health.* **2020**; 8:593256.
16. Guan WJ, Liang WH, Zhao Y, *et al.* Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J.* **2020**; 55(5):2000547

17. Kuderer NM, Choueiri TK, Shah DP, et al. Sex-bias in COVID-19-associated illness severity and mortality in cancer patients: a systematic review and meta-analysis. *E Clinical Medicine*. **2020**; 26:100519
18. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its impact on patients with COVID-19. *SN Compr Clin Med* **2020**; 2(30):1–8
19. Sanyaolu A, Okorie C, Marinkovic A. COVID-19 in cancer patients: clinical characteristics and outcome— an analysis of the LEOSS registry. *Ann Hematol*. **2021**;100(2):383–393
20. Lv Z, Lv S. Clinical characteristics and analysis of risk factors for disease progression of COVID-19: A retrospective Cohort Study. *Int J Biol Sci*. 2021 Jan 1;17(1):1-7.
21. Surendra H, Elyazar IR, Djaafara BA, et al. Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study. *Lancet Reg Health West Pac*. **2021**; 9:100108.
22. He YZ, Xie M, Zhao JP, et al. Clinical Characteristics and Outcomes of Patients with Severe COVID-19 and Chronic Obstructive Pulmonary Disease (COPD). *Med Sci Monit*. **2020**; 26: e927212
23. Castelnuovo AD, Bonaccio M, Costanzo S, et al. Common cardiovascular risk factors and in-hospital mortality in 3,894 patients with COVID-19: survival analysis and machine learning-based findings from the multicentre Italian CORIST Study. *Nutr Metab Cardiovasc Dis*. **2020**;30(11):1899-1913.

Tables

Table 1. Baseline information ($n=718$)

Variables	$\bar{x} \pm SD$ or case (%)	range
Age (years)	38.48 \pm 14.15	0.17~87
Male (case, %)	529(73.68)	
Duration (day)	1.74 \pm 1.20	1~30
Virus negative conversion time(day)	15.48 \pm 11.18	2~53
In-hospital time(day)	18.28 \pm 11.16	2~56
Disease severity		
Non-severe (case, %)	681(94.85)	
Severe (case, %)	37 (5.15)	
Prognosis		
Survival (case, %)	710(98.89)	
Death (case, %)	8(1.11)	

Table 2. Comparison of age and comorbidities between the non-severe group and the severe group ($n=718$)

variable	Non-severe group (n=681)	severe group (n=37)	<i>t</i> score or χ^2 score	<i>P</i> score
Age (year)	37.44±13.14	57.70±18.08	<i>t</i> =-8.940	<0.001
Number of comorbidities	1.19±1.12	2.53±0.94	<i>t</i> =-7.027	<0.001
Hypertension (case, %)	76(11.16)	6(16.22)	χ^2 =-0.141	0.347
Hyperlipidaemia (case, %)	129(18.94)	4(10.81)	χ^2 =-1.239	0.215
Hyperuricaemia and gout (case, %)	45(6.61)	2(5.41)	χ^2 =-0.288	0.773
Non-alcoholic fatty liver disease (case, %)	290(42.58)	14(37.84)	χ^2 =-0.569	0.570
Diabetes mellitus (case, %)	59(8.66)	4(10.81)	χ^2 =-0.449	0.653
Chronic hepatitis B (case, %)	56(8.22)	3(8.11)	χ^2 =-0.025	0.980
Chronic obstructive pulmonary disease (case, %)	13(1.91)	2(5.41)	χ^2 =-1.447	0.148
Chronic kidney disease (case, %)	9(1.32)	1(2.70)	χ^2 =-0.698	0.485
Cardiovascular diseases (case, %)	12(1.76)	2(5.41)	χ^2 =-1.560	0.119
Cancer (case, %)	18(2.62)	0(0.00)	χ^2 =-1.001	0.317
Other (case, %)	49(7.20)	3(8.11)	χ^2 =-0.208	0.835

Table 3. Comparison of age and comorbidities between the survival group and the non-surviving group (*n*=718)

variable	survival group (n=710)	dead group (n=8)	t score or χ^2 score	P score
Age (year)	38.10±13.67	77.14±6.69	t=-7.543	<0.001
Number of comorbidities	1.24±1.13	3.00±0.00	t=-4.075	<0.001
Hypertension (case, %)	79 (11.13)	3(37.50)	χ^2 =-2.626	0.009
Hyperlipidaemia (case, %)	133(18.73)	0(0.00)	χ^2 =-1.267	0.205
Hyperuricaemia and gout (case, %)	47(6.62)	0(0.00)	χ^2 =-0.703	0.482
Non-alcoholic fatty liver disease (case, %)	301(42.39)	3(37.50)	χ^2 =-0.028	0.978
Diabetes mellitus (case, %)	63(8.87)	0(0.00)	χ^2 =-0.824	0.410
Chronic hepatitis B (case, %)	58(8.17)	1(12.50)	χ^2 =-0.587	0.557
Chronic obstructive pulmonary disease (case, %)	15(2.11)	0(0.00)	χ^2 =-0.388	0.698
Chronic kidney disease (case, %)	9(1.27)	1(12.50)	χ^2 =-2.923	0.003
Cardiovascular diseases (case, %)	13(1.83)	1(12.50)	χ^2 =-2.370	0.018
Cancer (case, %)	18(2.54)	0(0.00)	χ^2 =-0.426	0.670
Other (case, %)	52(7.32)	0(0.00)	χ^2 =-0.742	0.408

Table 4. Spearman correlation analysis of disease severity, virus negative conversion time, prognosis, age and comorbidities (n=718)

variable	disease severity (1=non-severe,2=severe)		virus negative conversion time(days)		Prognosis (1=survival,2=death)	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Age(year)	0.158	0.000	0.189	0.000	0.105	0.018
Number of comorbidities (0,1,2,3and more)	0.238	<0.001	0.225	<0.001	0.140	<0.001
Non-alcoholic fatty liver disease (1=without,2=with)			0.114	0.002		
Chronic hepatitis B (1=without,2=with)			0.089	0.017		
Chronic obstructive pulmonary disease (1=without,2=with)			0.077	0.039		
Chronic kidney disease (1=without,2=with)					0.101	0.007
Cardiovascular diseases (1=without,2=with)					0.081	0.030
Hypertension (1=without,2=with)					0.087	0.020

Table 5. Multiple stepwise regression analysis of influencing factors for disease severity, clinical classification, coronavirus negative conversion time and prognosis ($n=718$)

independent variable		B	Std. Error	Beta	t	P
Disease severity (1=non-severe,2=severe)	constant	0.989	0.012	-	84.1	<0.001
	age	0.001	0.000	0.127	2.660	0.008
	Number of comorbidities (0,1,2,3and more)	0.048	0.007	0.254	7.027	<0.001
	Hyperlipidaemia (1=without,2=with)	-0.043	0.021	-0.077	-2.118	0.035
Virus negative conversion time (day)	constant	13.051	0.635	-	20.543	<0.001
	Number of comorbidities (0,1,2,3and more)	1.971	0.342	0.213	5.766	<0.001
	Hyperlipidaemia (1=without,2=with)	-2.793	1.023	-0.102	-2.729	0.007
	Non-alcoholic fatty liver disease (1=without,2=with)	2.121	0.806	0.099	2.631	0.009
	Chronic obstructive pulmonary disease (1=without,2=with)	5.566	2.691	0.075	2.068	0.039
Prognosis (1=survival,2=death)	constant	0.992	0.025	-	183.925	<0.001
	Number of comorbidities (0,1,2,3and more)	0.013	0.003	0.148	4.024	<0.001
	Chronic kidney disease (1=without,2=with)	0.088	0.031	0.105	2.864	0.004

Table 6. the performance of various methods for distinguishing between the severe cases and the non-severe patients (n=718)

variables	Cutoff point	AUC (95%CI)	Sensitivity	Specificity	False positive	False negative
Number of comorbidities	3.5	0.864(0.793~0.935)	75.70%	88.00%	24.30%	12.00%

Abbreviations: AUC, area under the curve; CI, confidence interval.

Table 7. the performance of various methods for distinguishing between the dead cases and the survived patients (n=718)

variables	Cutoff point	AUC (95%CI)	Sensitivity	Specificity	False positive	False negative
Number of comorbidities	4.5	0.947(0.893~1.000)	85.70%	91.60%	14.30%	8.40%

Abbreviations: AUC, area under the curve; CI, confidence interval.

Figures

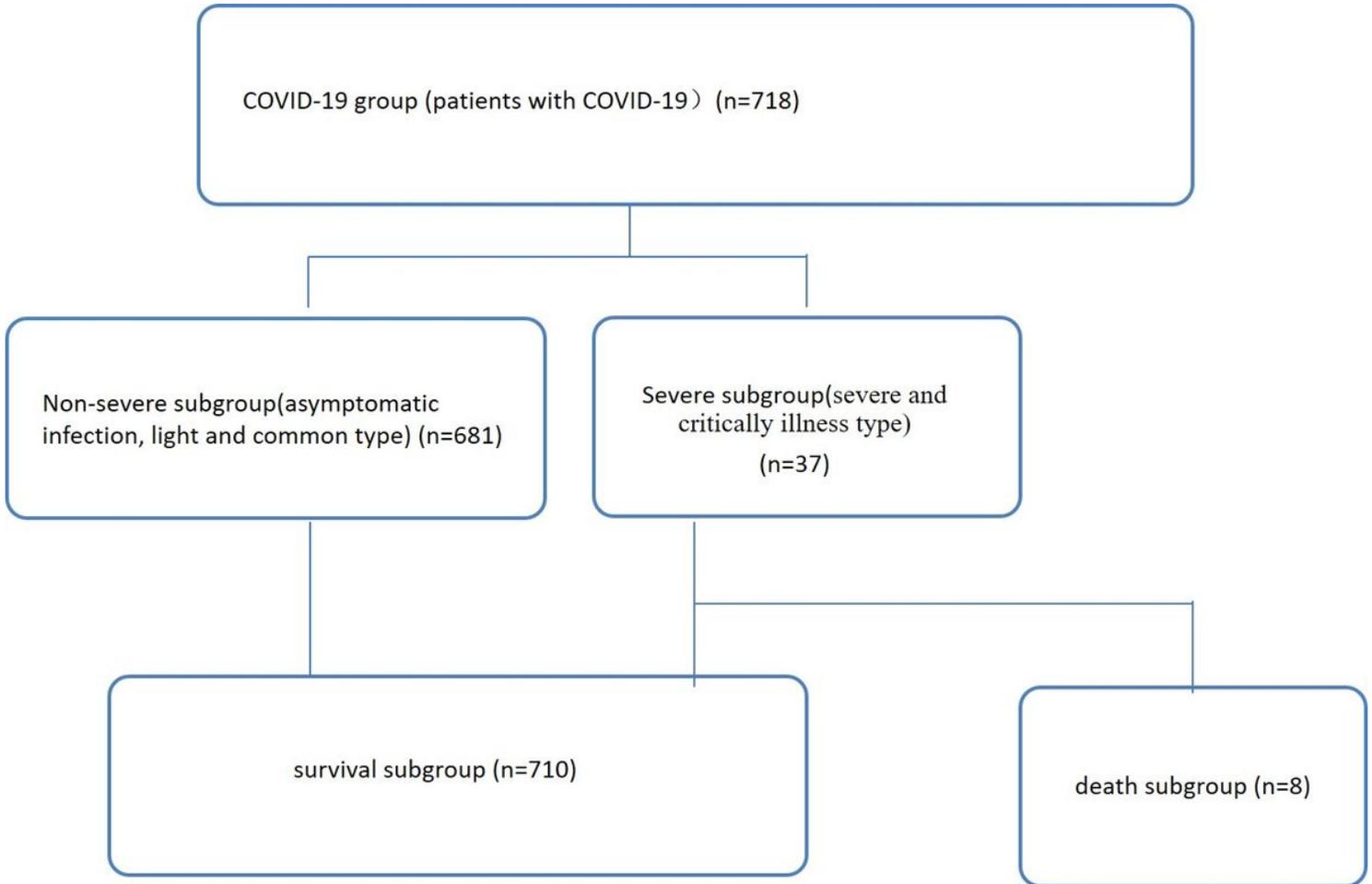


Figure 1

Patient data (n=718). Non-severe refers to the clinical type of COVID-19 that is asymptomatic, light and common. Severe refers to the clinical type of COVID-19 that is associated with severe and critical illness.

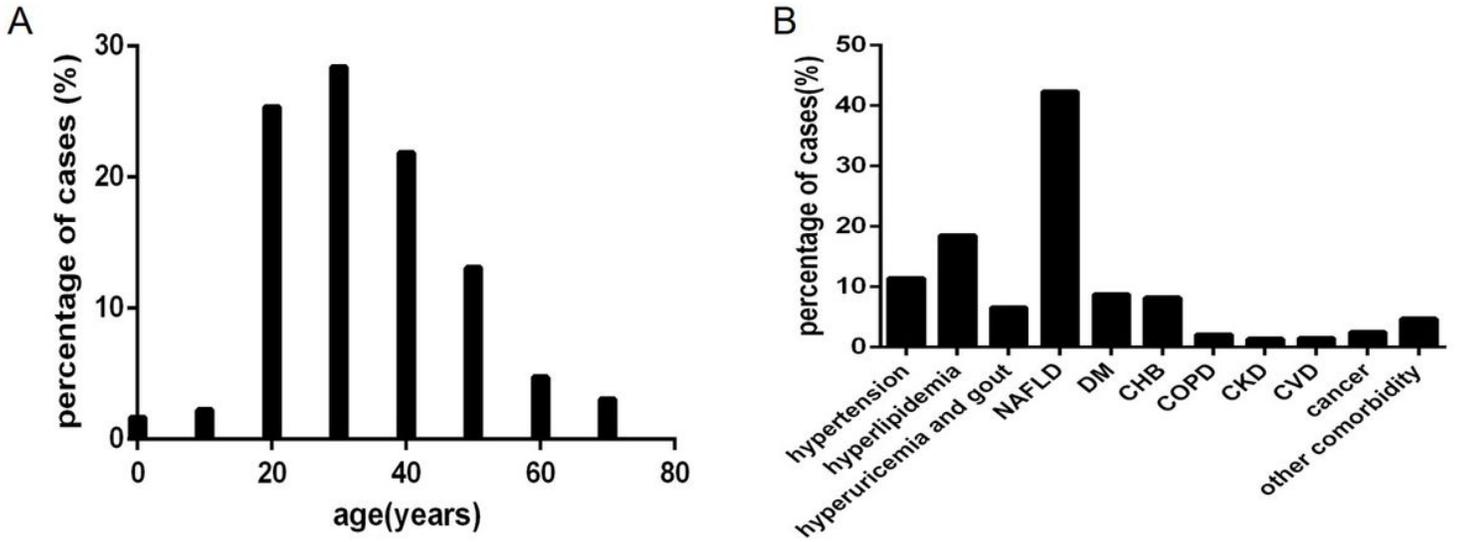


Figure 2

The distribution characteristics of age and comorbidities in COVID-19 patients (n=718). Abbreviations: COVID-19, coronavirus disease 2019. A. age. B. comorbidity.

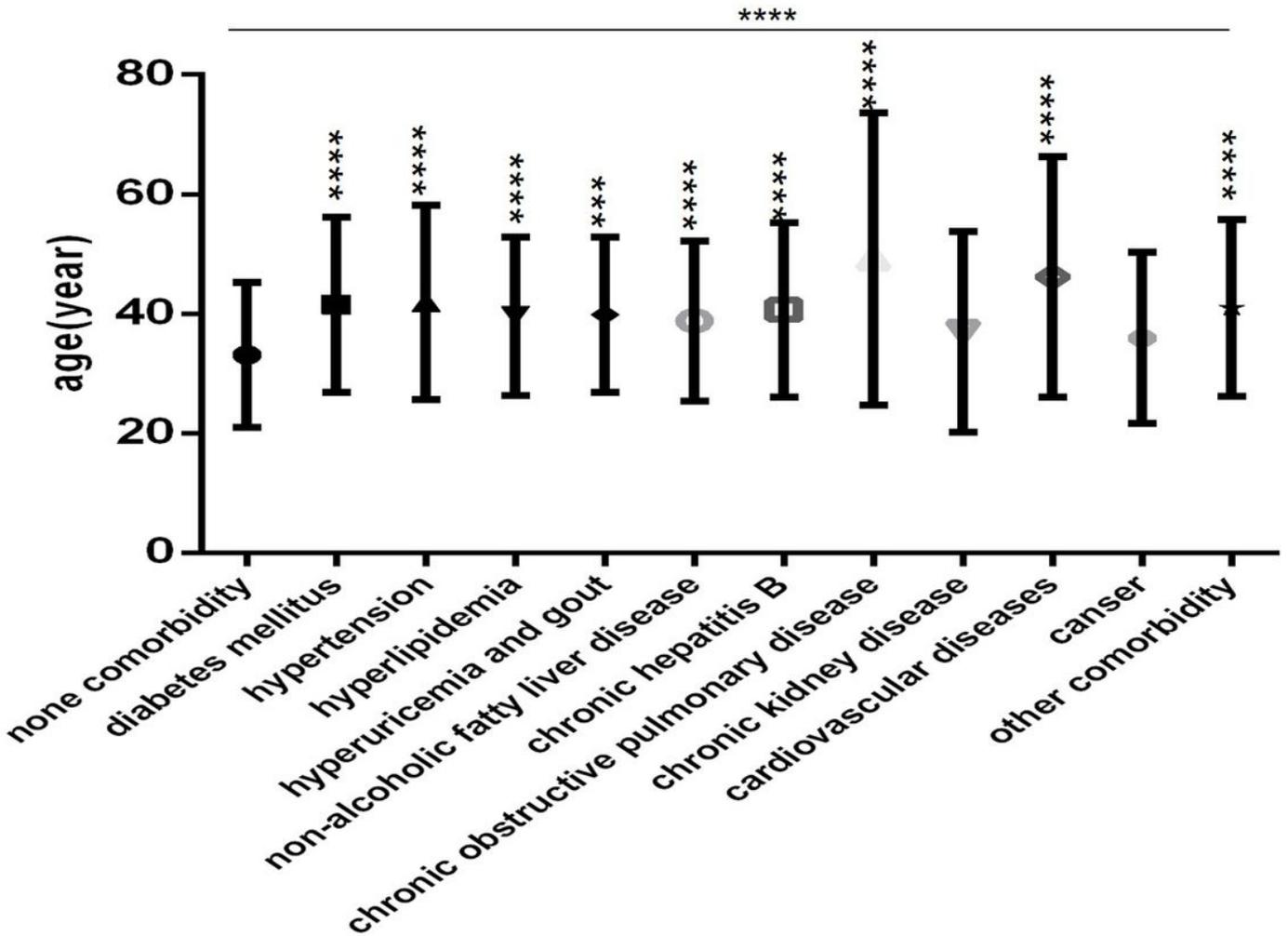


Figure 3

Comparison of age among the no comorbidity group and each comorbidity group (n=718; 0, 1, 2, 3 or more comorbidities groups, n=253, 193, 127 and 145, respectively). Abbreviations: COVID-19, coronavirus disease 2019. Unpaired one-way ANOVA was used for intergroup comparisons ($P < 0.0001$). Unpaired t-tests were used for comparisons with the control group, $***P < 0.001$, $****P < 0.0001$.

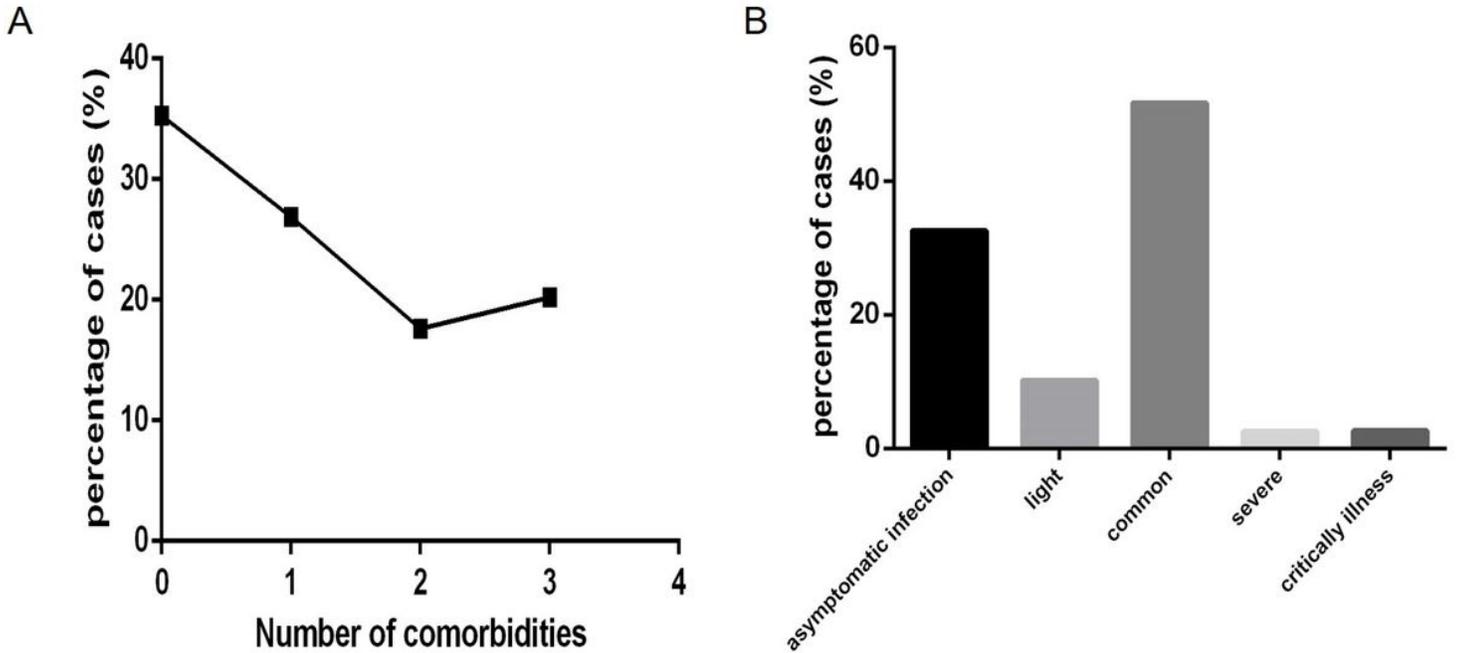


Figure 4

The distribution of patients with severe COVID-19 and who died in different age-interval groups (n=718). Abbreviations: COVID-19, coronavirus disease 2019. A. severe cases. B. dead cases.

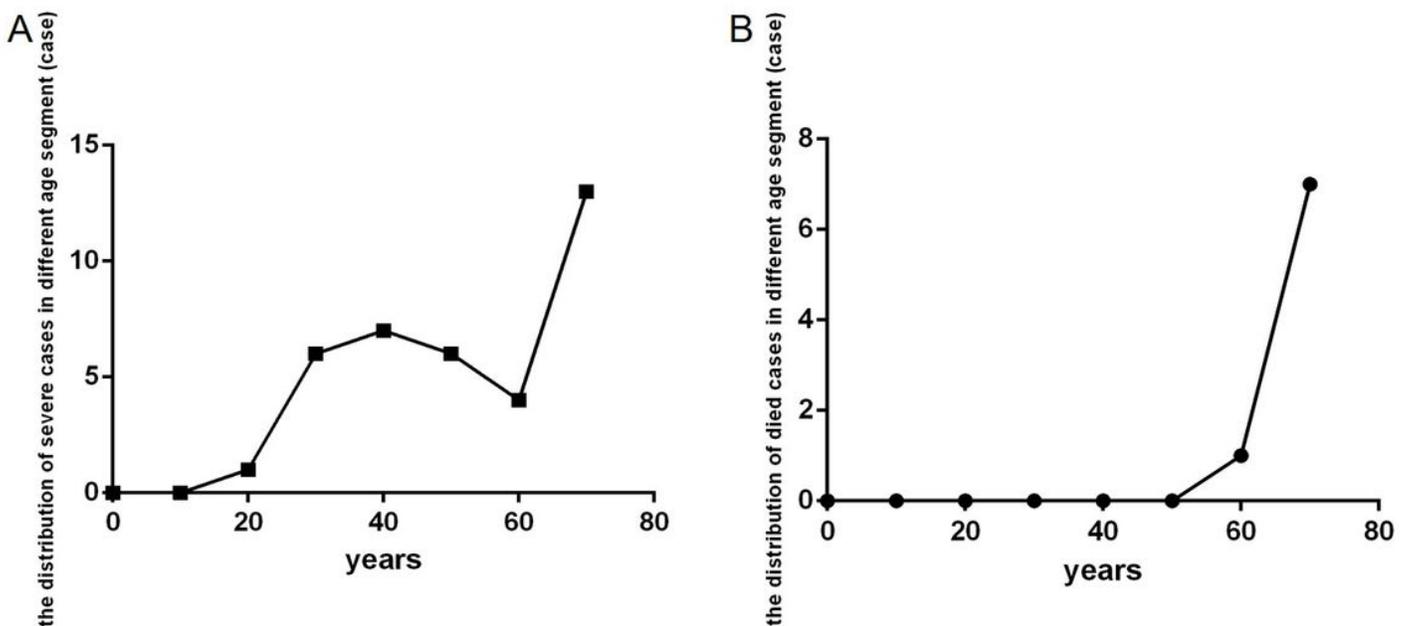


Figure 5

The distribution characteristics of the number of comorbidities and clinical type among COVID-19 patients (n=718). Abbreviations: COVID-19, coronavirus disease 2019. A. number of comorbidities. B. clinical type.

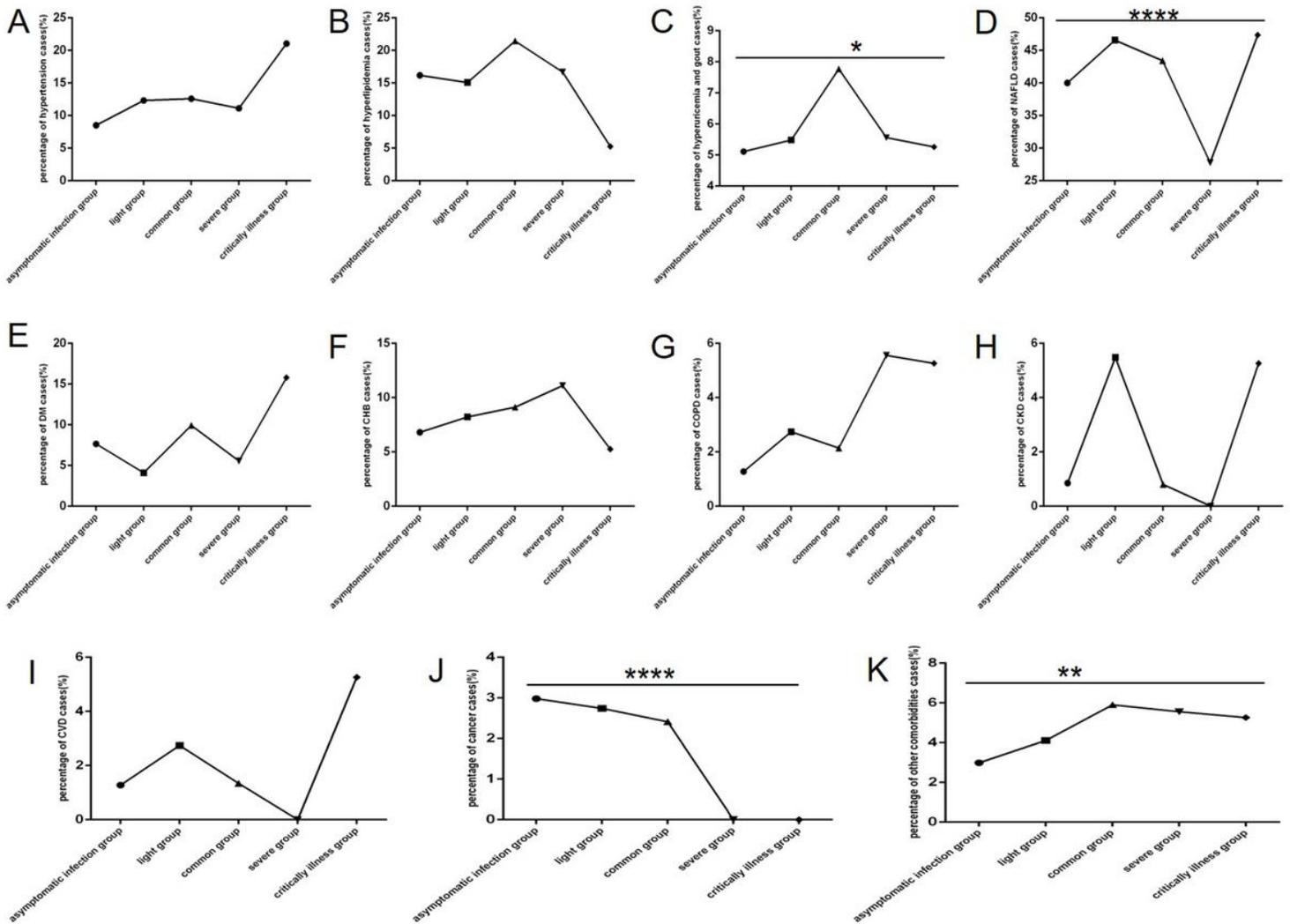


Figure 6

Comparison of the percentage of each comorbidity case among different clinical type groups (n=718; asymptomatic infection, light, common, severe and critically ill groups, n=234, 73, 371, 18 and 19, respectively). Abbreviations: COVID-19, coronavirus disease 2019; NAFLD, non-alcoholic fatty liver disease; DM, diabetes mellitus; CHB, chronic hepatitis B; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CVD, cardiovascular disease. A. Hypertension. B. Hyperlipidaemia. C. Hyperuricaemia and gout. D. NAFLD. E. DM. F. CHB. G. COPD. H. CKD. I. CVD. J. Cancer. K. Other. Unpaired one-way ANOVA was used for intergroup comparisons (D, J, P all<0.0001; K, P all<0.01; C, P <0.05; A, B, E, F, G, H, I, all P>0.05).

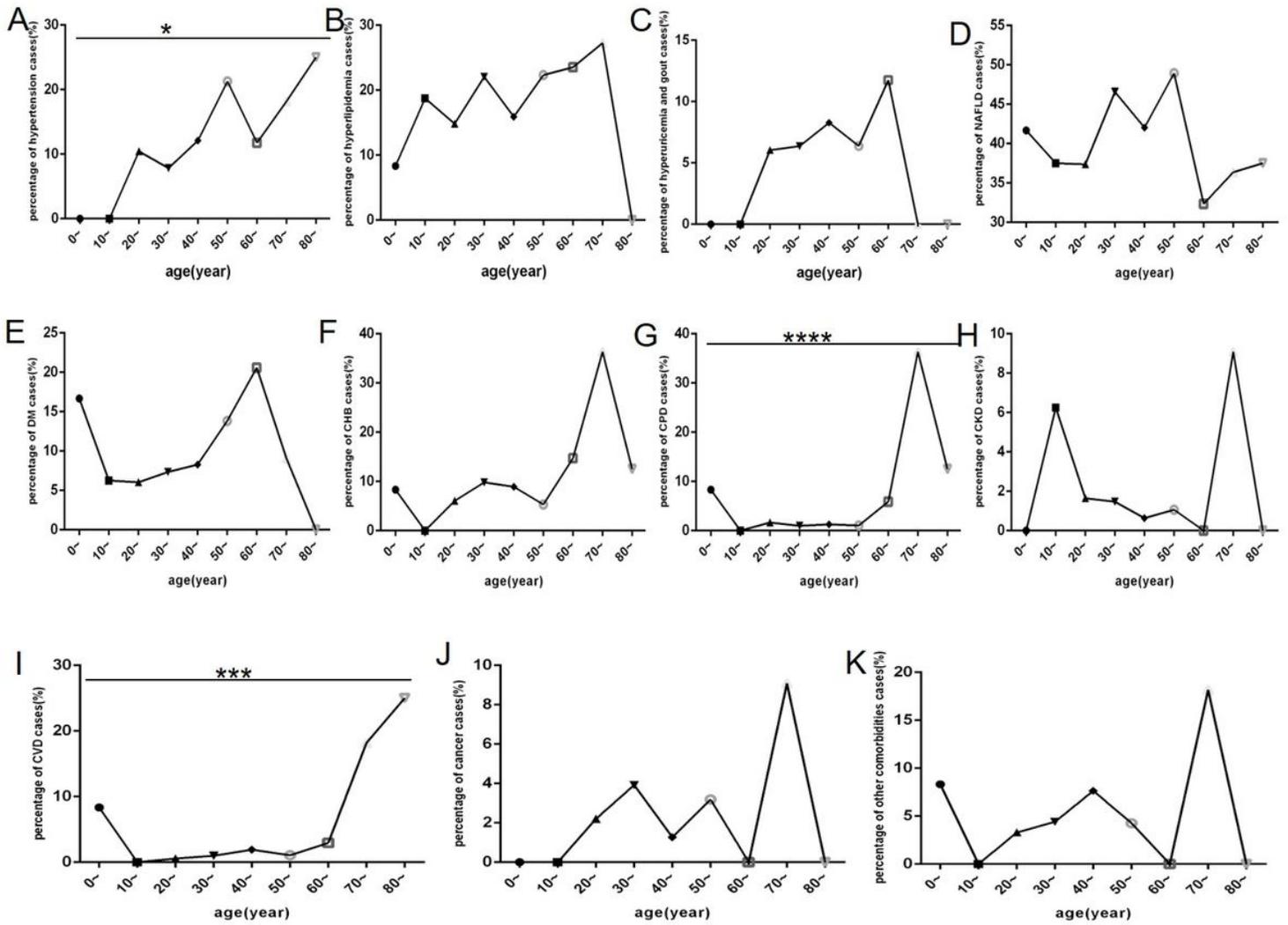


Figure 7

Comparison of the percentage of each comorbidity case among different age-interval groups (n=718). Abbreviations: COVID-19, coronavirus disease 2019; NAFLD, non-alcoholic fatty liver disease; DM, diabetes mellitus; CHB, chronic hepatitis B; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CVD, cardiovascular disease. A. Hypertension. B. Hyperlipidaemia. C. Hyperuricaemia and gout. D. NAFLD. E. DM. F. CHB. G. COPD. H. CKD. I. CVD. J. Cancer. K. Other. Unpaired one-way ANOVA was used for intergroup comparisons (G, $P < 0.0001$; I, $P < 0.001$; A, $P < 0.05$; B, C, D, E, F, H, J, K, all $P > 0.05$).

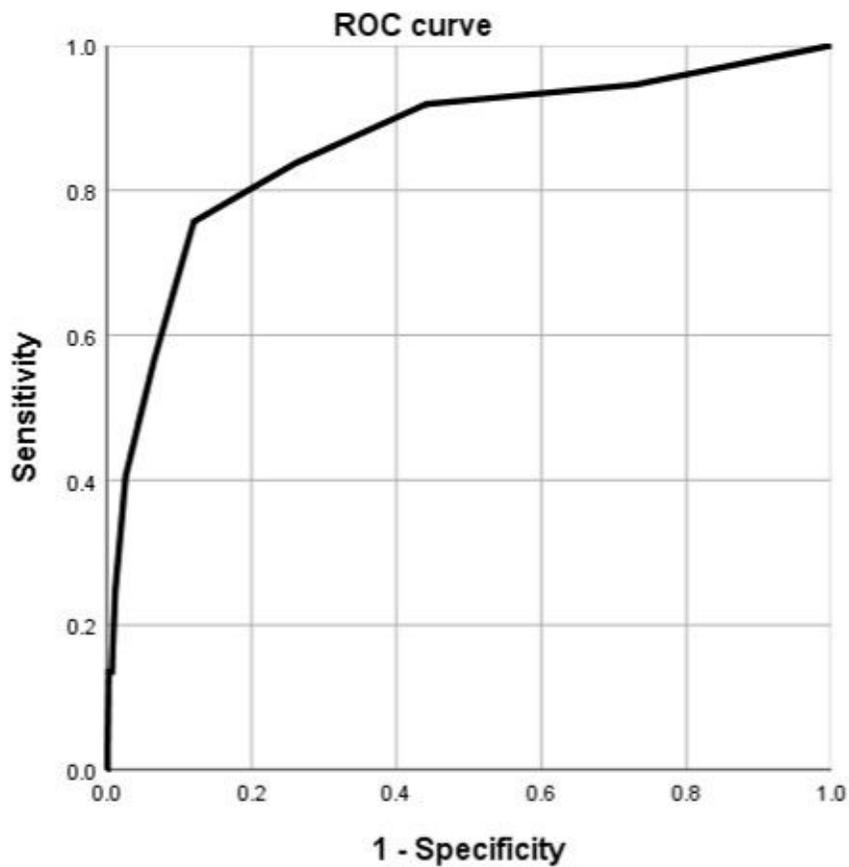


Figure 8

Using number of comorbidities for discriminating the severe cases from the nonsevere patients (n=718; non-severe and severe groups, n=681 and 37, respectively). ROC analysis showing the performance of number of comorbidities in distinguishing severe cases from nonsevere patients. Abbreviations: ROC, receiver operating characteristic curve; AUC, area under the curve.

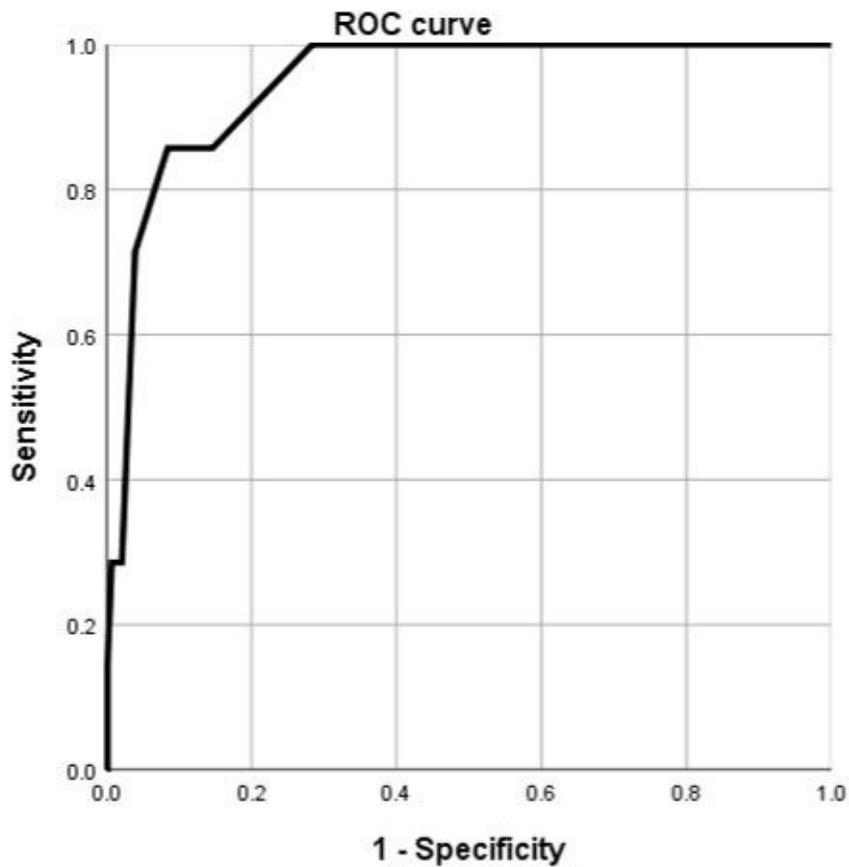


Figure 9

Using number of comorbidities for discriminating the dead cases from the surviving patients (n=718; survival and dead groups, n=710 and 8, respectively). ROC analysis showing the performance of number of comorbidities in distinguishing the dead cases from the surviving patients. Abbreviations: ROC, receiver operating characteristic curve; AUC, area under the curve.