Comorbidities Associated with Complicated Hospital Course and Death in COVID-19 Patients: A Retrospective Study from Iran

Nader Tavakoli

Iran University of Medical Sciences

Nahid Hashemi-Madani

Iran University of Medical Sciences

Mojtaba Malek

Iran University of Medical Sciences

Zahra Emami

Iran University of Medical Sciences

Alireza Khajavi

Shahid Beheshti University of Medical Sciences

Rokhsareh Aghili

Iran University of Medical Sciences

Maryam Honardoost

Iran University of Medical Sciences

Fereshteh Abdolmaleki

Iran University of Medical Sciences

Mohammad Ebrahim Khamseh (✉ khamseh.m@iums.ac.ir)

Iran University of Medical Sciences

Research Article

Keywords: COVID-19, Comorbidity, Invasive ventilation, Mortality, Iran

Posted Date: December 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1036149/v1>

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

Abstract

Objective There are limited data regarding the impact of comorbidities on hospitalized patients with coronavirus disease 2019 (COVID-19) in Iran.

Methods We evaluated the risk of serious adverse outcomes in 1368 Iranian COVID-19 patients, admitted to five academic hospitals in Tehran between February-June 2020. The composite end-points were defined as admission to an intensive care unit, invasive ventilation, or death. The Cox proportional survival model determined the potential comorbidities associated with death.

Results Overall, 576 patients (42.3%) reached the composite end-point (280 death). Adjusted for age, sex, duration of hospitalization, and the presence of the other comorbidities, patients with diabetes (RR=1.25, 95%CI; 1.08-1.44), heart failure (RR=1.45, 95%CI; 1.10-1.91), chronic kidney disease (RR=1.32, 95%CI; 1.04-1.67), malignancy (RR=1.79, 95%CI; 1.41-2.28), and lung diseases (RR=1.53, 95%CI; 1.27-1.84) were more likely to reach the composite end-point than those without the very comorbidity. Moreover, patients aged less than 65 years had a greater risk of death in the presence of two (HR=2.68, 95%CI; 1.46-4.95, $p=0.002$) or more (HR=3.47, 95%CI; 1.69-7.12, $p=0.001$) comorbidities, compared to those without any comorbidity.

Conclusion To conclude, having two or more comorbidities in patients less than 65 years is associated with a greater risk of death during hospitalization.

Introduction

The novel coronavirus SARS-CoV-2, presenting with heterogeneous clinical manifestations [1–3], easily predisposes the susceptible patients to the respiratory failure and death [1, 4, 5]. Previous studies have demonstrated such underlying chronic disease as diabetes mellitus (DM), hypertension (HTN), cardiovascular disease (CVD), and chronic obstructive pulmonary disease (COPD) are more likely to complicate the clinical course of coronavirus disease 2019 (COVID-19) [6, 7]. The affected patients are at a greater risk of developing respiratory failure, admitting to an intensive care unit (ICU), and eventually death [3, 8, 9]. However, there are significant differences in population demographics, smoking rates, and prevalence of comorbidities among the countries [10, 11]. Thus, comprehensive reports on early clinical outcomes of COVID-19 from involved patients of various ethnicities seem to be essential for identification of the sub-populations with poorer prognosis.

The first confirmed case of COVID-19 in Iran was reported from Qom in February 2020 [12]. Soon after, Tehran and the other provinces reported outbreak, and now Iran ranked the tenth position globally [13]. Few studies investigating the association of some underlying chronic diseases and COVID-19 in Iran have certain limitations including the relatively small sample size and being single center observation [14]. On the other hand, the rate of infection in Tehran, with its high population density, has exceeded every other province [15]. This study evaluates the early clinical course of patients with COVID-19 hospitalized at several academic centers in Tehran, stratified by the number and type of comorbidities.

Materials And Methods

Data source and data collection

This is a retrospective cohort study conducted at 5 academic hospitals affiliated to Iran Universities of Medical Sciences (IUMS) in Iran. The study was approved by the ethics committee of the IUMS. Considering the minimal-risk research using data collected in routine clinical practice, the requirement for informed consent was waived. We enrolled all hospitalized patients with confirmed COVID-19 admitted between February 20, 2020 and June 13, 2020. Patients were considered to have confirmed COVID-19 if the polymerase chain reaction (PCR) assay of a nasopharyngeal specimen was positive. Those without laboratory documents for COVID-19 who presented the clinical manifestations of COVID-19 along with typical chest computed tomography (CT) findings were also considered as having COVID-19. For patients with a readmission during the study period, data from the first admission are presented.

Medical records of all admitted patients including demographic data, smoking status, vital signs at the time of admission, baseline comorbidities, chest CT findings, as well as hospital course data including admission to ICU, treatment with invasive mechanical ventilation, duration of hospitalization, and patient status at the time of discharge (alive or dead) were collected. All clinical profiles from five academic hospitals were centrally merged. Some experienced technicians entered data into a computerized database for further double checking of all cases.

Comorbidities were determined based on patients' self-report on admission. A total of 8 comorbidities, namely DM, HTN, coronary artery disease (CAD), chronic kidney disease (CKD), heart failure (HF), lung diseases including asthma and COPD, cerebrovascular accidents (CVA), and malignancy, were included in the final analysis. Comorbidities were initially considered as a categorical variable (yes versus no) and subsequently classified based on the number (single versus multiple).

Admission to ICU, treatment with invasive mechanical ventilation, and death were the primary outcomes of this study measured individually and as a composite outcome. All clinical outcomes are presented for patients who completed their hospital course (discharged alive or dead).

Statistical analysis

The continuous variables are presented as median (interquartile ranges (IQR)), and the categorical ones are presented as the number and (percentages).

To measure the impact of each of the eight mentioned comorbidities on the occurrence of either of the response variables namely death, ICU admission, invasive mechanical ventilation, and the composite outcome, the adjusted risk ratios were computed, applying the method suggested by Norton et al (2013), adjusted for age, sex, duration of hospitalization, and the other comorbidities [16].

Finally, a survival analysis was performed to estimate the probability of death from the date of hospital admission. For this purpose, the Kaplan-Meier survival curve was drawn separately for the patients with 0, 1, 2, or ≥ 3 comorbidities, and the Log-rank test assessed the difference between these categories. Then, the cox proportional hazard survival models were fitted at the hospitalization times to obtain the hazard ratios of death between those with and without any of the eight mentioned comorbidities. These models were adjusted for age, sex, and the other comorbidities. Statistical analyses were performed applying Stata software (version 13). The significant level was set as 0.05.

Results

Baseline characteristics and comorbidities

This multicenter retrospective cohort study included 1368 (59.9% men) hospitalized COVID-19 patients with median age of 58 (IQR; 43-70) years. Comorbidity were recorded in 1235 individuals, of whom 633 (51.3%) reported having at least one comorbidity (26.6% one comorbidity, 15.1% two comorbidities, and 9.6% more than two comorbidities). The prevalence of specific comorbidities was as follow: DM (n= 362, 26.5%), HTN (n= 359, 26.2%), CAD (n= 99, 7.2%), HF (n= 44, 3.2%), CVA (n= 40, 2.9%), CKD (n= 67, 4.9%), malignancy (n= 37, 2.7%), lung disease including asthma (n= 41, 3.0%) and COPD (n=43, 3.1%), chronic liver disease (n=14, 1.0%), Tuberculosis (TB) (n= 9, 0.7%), and human immunodeficiency virus (HIV) (n= 3, 0.2%). Baseline and clinical characteristics of the hospitalized patients including sex, age, smoking status, opium addiction, as well as temperature, respiratory rate, systolic and diastolic blood pressure, and the presence of abnormal chest CT findings at the time of admission, stratified by the type of comorbidity, are presented in Table 1.

Table 1

Baseline and clinical characteristics of patients hospitalized with COVID-19 stratified by different types of comorbidities.

Variability	DM n=362	HTN n=359	CAD n=99	HF n=44	CVA n=40	CKD n=67	Malignancy n=37	Lung disease n=78	No comorbidity n=602
Sex (Male)	205/362 (56.6)	194 /359 (54.0)	61 /99 (61.6)	26 /44 (59.1)	25 /40 (62.5)	37 /67 (55.2)	21 /37 (56.8)	50/78 (64.1)	362/602(60.1)
Age (yrs)	65 (56-74)	69 (60-78)	70 (60- 77)	75 (65- 81)	70 (61- 75)	68 (55- 77)	65 (57-76)	64 (53-72)	49 (38-62)
Smoking	283/297 (95.3)	276/289 (95.5)	74/82 (90.2)	36 /36 (100)	32/36 (88.9)	47/49 (95.9)	34 /36 (94.4)	49 /49 (86.0)	585/595 (98.3)
No/unknown	14/297 (4.7)	13/289 (4.5)	8/82 (9.8)	0 /36 (0.0)	4 /36 (11.1)	2 /49 (4.1)	2/36 (5.6)	8/49 (14.0)	10/595(1.7)
Former/current									
Opium addiction (yes)	8/253 (3.2)	9 /237 (3.8)	4 /62 (6.5)	0/25 (0.0)	1 /16 (6.3)	2 /38 (5.3)	1/20 (5.0)	3 /45 (6.7)	6/591 (1.0)
T on admission	37 (36.8- 37.5)	37 (37- 37.5)	37 (36.9- 37.5)	37.1 (36.8- 37.5)	37 (36.9- 37.5)	37 (36.8- 37.5)	37 (36.9-37.7)	37.2 (37- 37.6)	37.1 (36.9-37.5)
RR on admission	18 (17-20)	18 (17-20)	18 (17- 20)	18 (16- 20)	18 (17- 22)	18 (16- 20)	18 (18-21)	18 (17-20)	18 (16-20)
SBP on admission	120 (110- 130)	120 (114- 130)	120 (110- 130)	123 (115- 135)	135 (120- 148)	120 (110- 130)	111 (101-128)	120 (112- 130)	120 (110-124)
DBP on admission	75 (70-80)	80 (70-80)	79 (70- 80)	80 (70- 84)	80 (70- 85)	76 (68- 80)	70 (60-80)	80 (70-85)	80 (70-80)
Abnormal chest CT(yes)	279/287 (97.2)	280/287 (97.6)	69 /74 (93.2)	28 /29 (96.6)	34 /36 (94.4)	45/48 (93.8)	28/29 (96.6)	61 /63 (96.8)	396/435 (91.0)
Data are presented as median (IQR), or n/N (%); N is the total number of patients with available data. DM ; Diabetes mellitus, HTN; Hypertension, CAD; Coronary artery disease, HF; Heart failure, CVA; Cerebrovascular accident, CKD; Chronic kidney disease, T; temperature, RR; respiratory rate, SBP; systolic blood pressure, DBP; diastolic blood pressure, CT; computed topography.									

Outcomes during the hospital course

Of the 1368 hospitalized patients, 414 (33.0%) individuals were admitted to ICU, 237 (18.0%) individuals received invasive mechanical ventilation, and eventually 280 (20.6%) individuals died during the hospital course. Outcomes stratified by the presence or absence of any comorbidity are presented in Supplementary Figure 1. Compared to the patients without any comorbidity, those who reported at least one comorbidity were more likely to be admitted to ICU (48.3% versus 19.0%), receive invasive mechanical ventilation (23.8% versus 14.2%), and die (30.2% versus 12.6%).

Prognostic analyses

The individual impact of any comorbidity on the outcomes is presented in Table 2. Having been adjusted for age, sex, duration of hospitalization, and the presence of the other comorbidities, patients with DM (RR; 1.25, 95% CI; 1.08-1.44), HF (RR; 1.45, 95% CI; 1.10-1.91), CKD (RR; 1.32, 95% CI; 1.04-1.67), malignancy (RR; 1.79, 95% CI; 1.41-2.28), and lung diseases (RR; 1.53, 95% CI; 1.27-1.84) were more likely to reach the composite end-point than those without the very comorbidity. We further evaluated the impact of any type of comorbidity on the individual clinical outcomes during the hospital course. After adjusting for age, sex, duration of hospitalization, and the presence of the other comorbidities, patients with DM (RR; 1.31, 95% CI; 1.09-1.56), CAD (RR; 1.37, 95% CI; 1.08-2.73), CVA (RR; 1.52, 95% CI; 1.02-2.25), malignancy (RR; 1.98, 95% CI; 1.44-2.71), and lung disease (RR; 1.72, 95% CI; 1.35-2.19) were more likely to be admitted to ICU, those with HTN (RR; 1.40, 95% CI; 1.06-1.85) and malignancy (RR; 1.64, 95% CI; 1.01-2.66) were more likely to receive invasive mechanical ventilation, and the patients with DM (RR; 1.50, 95% CI; 1.20-1.89), CKD (RR; 2.03, 95% CI; 1.49-2.76), malignancy (RR; 2.50, 95% CI; 1.74-3.61), and lung disease (RR; 1.63, 95% CI; 1.20-2.21) were more likely to die, comparing to their counterparts without the very comorbidity.

Table 2
Comorbidities associated with complicated hospital course in COVID-19 hospitalized patients.

	*Composite end-point	Death	ICU admission	Invasive ventilation
	RR(95%CI)	RR(95%CI)	RR(95%CI)	RR(95%CI)
DM	1.25 (1.08-1.44)	1.50 (1.20-1.89)	1.31 (1.09-1.56)	1.04 (0.80-1.37)
HTN	1.10 (0.95-1.28)	1.21 (0.95-1.53)	1.14 (0.95-1.36)	1.40 (1.06-1.85)
CAD	1.07 (0.86-1.32)	1.00 (0.70-1.43)	1.37 (1.08-1.73)	0.71 (0.44-1.14)
HF	1.45 (1.10-1.91)	1.24 (0.83-1.87)	1.28 (0.95-1.71)	1.34 (0.78-2.31)
CVA	1.08 (0.74-1.56)	1.11 (0.65-1.87)	1.52 (1.02-2.25)	0.77 (0.38-1.54)
CKD	1.32 (1.04-1.67)	2.03 (1.49-2.76)	1.30 (0.98-1.72)	0.61 (0.33-1.12)
Malignancy	1.79 (1.41-2.28)	2.50 (1.74-3.61)	1.98 (1.44-2.71)	1.64 (1.01-2.66)
Lung disease	1.53 (1.27-1.84)	1.63 (1.20-2.21)	1.72 (1.35-2.19)	1.66 (0.85-1.88)
Adjusted for age, sex, duration of hospitalization, and other comorbidities. DM ; Diabetes mellitus, HTN; Hypertension, CAD; Coronary artery disease, HF; Heart failure, CVA; Cerebrovascular accident, CKD; Chronic kidney disease. ICU; intensive care unit.				
*Composite end-point consisted any of death, ICU admission, or invasive ventilation.				

Survival analysis

We further investigated time-to-death during the hospital course separately for each type of comorbidity and the number of comorbidities. Kaplan-Meier survival curve demonstrates the probability of death during the hospital course in the patients with one, two, or more than two comorbidities (Figure 1). Cox proportional hazard regression models were applied to determine the type and the number of comorbidities associated with death during the hospital course (Figures 2). Having been adjusted for age, sex, and the other comorbidities, patients with DM (HR; 1.47, 95% CI; 1.10-1.95, $p=0.008$) and CKD (HR; 1.72, 95% CI; 1.16-2.56, $p=0.007$) showed a significant increase in the hazard of occurrence of death during the hospital course, compared to those without DM or CKD, respectively. Moreover, compared to the patients with no comorbidity, those with two comorbidities (HR; 1.54, 95% CI; 1.05-2.27, $p=0.02$) and three or more comorbidities (HR; 1.81, 95% CI; 1.22-2.70, $p=0.003$) were significantly at a greater risk of death during the hospital course. However, there was no significant difference in the hazard of death between patients with one comorbidity and those without any comorbidity (HR; 1.12, 95% CI; 0.77-1.62, $p=0.565$). Since age was a significant risk factor of poorer outcome in any type of the comorbidities, we further performed a sensitivity analysis stratifying the patients by age (< 65 vs ≥ 65 years). The results indicated a greater number of

comorbidities are associated with a significant increase in the hazard of death only in patients less than 65 years old. The results are shown in Figure 3.

Discussion

This retrospective study identified the type and number of comorbidities associated with a complicated hospital course and increasing risk of death in a large cohort of hospitalized Iranian patients with COVID-19. Patients with DM, HF, CKD, malignancy, and lung disease had significantly higher risks of reaching the composite end-point (ICU admission, invasive mechanical ventilation, or death). Moreover, those with DM and CKD had a significantly escalated risk of death during the hospital course. Considering the number of comorbidities, having two or more comorbidities incrementally increased the risk of death during the hospitalization in patients less than 65 years.

The most prevalent comorbidities in this large cohort of COVID-19 patients were DM, HTN, and CAD. These comorbidities remained the most common underlying diseases in the studies with different sample sizes conducted in various populations [1, 4, 17]. Moreover, meta-analyses of several studies, although most of them had been conducted in china, reported the same findings [18, 19]. Considering the relatively large sample size, we investigated a spectrum of comorbidities including CKD, HF, CVA, COPD, asthma, chronic liver disease, HIV, and TB. Consistent with the results of previous studies [1, 4, 17], the percentage of patients with these comorbidities was relatively low. This observation could be explained by the facts that such cardio-metabolic diseases as DM, HTN, and CAD are highly prevalent across the world, and they are more likely to be reported by the patients. Furthermore, the observed frequency of comorbidities might also be representative of the transmission of disease within the particular sub-groups.

Similar to the previous studies [17, 20, 21], our findings suggested that comorbidities such as malignancy, lung disease (COPD and asthma), HF, CKD, and DM are associated with a complicated hospital course in patients with COVID-19. However, in this cohort patients with known HTN did not reach the composite end-point. While HTN was associated with a significant greater risk of the same composite end-point in a large cohort of Chinese patients with COVID-19 [17]. This discrepancy might be explained by the fact that no adjustment for other comorbidities was made in this study while we considered all the other co-existence underlying disease such as malignancy, lung disease, HF, CKD, and DM that could confound the results. Moreover, patients in our cohort had well-controlled blood pressure (BP) at the time of admission (with median of 120/80 mmHg). This finding highlighted that poorly controlled BP might complicate the hospital course of COVID-19 patients not merely being known as a hypertensive case. Another meta-analysis that concluded HTN is associated with a greater risk of ICU admission had included studies with relatively low sample size not adjusted for other potential risk factors [8]. Moreover, definition of HTN and the need for ICU admission were different in the included studies [8].

Survival analysis showed DM and CKD significantly increased the hazard of death during the hospital course. Not only did previous studies indicate DM is associated with an increase in the risk of mortality [22, 23] but also they indicated different levels of blood glucose control impose different outcomes in patients with COVID-19 and preexisting T2DM [24]. Although some studies found an adverse association between CKD and severity of COVID-19 [20], few investigated the impact of CKD on the death [25]. On the contrary to the study conducted in New York [25] we found a significant association between CKD and the death in the hospitalized patients, considering all the potential risk factors. This inconsistency might be explained by the fact that the previous study was a single center one that had not included a large number of patients. Moreover, a prospective study, although included a small number of patients with known CKD (2.0%), demonstrated a significant association between kidney disease and in-hospital death [26].

Although the coexistence of different underlying diseases has been frequently reported in the cohorts of COVID-19- patients [4, 21, 27], a few investigated the impact of coexisting comorbidities on the clinical outcome of COVID-19 [17]. Our study confirmed the coexistence of two or more comorbidities incrementally increased the hazard of the death. However, there was no significant difference in the prognosis of those with one comorbidity compared to the ones without any comorbidity. Considering the strong independent role of age in the complicated hospital course and in-hospital death [14, 25], we

performed a sensitivity analysis stratifying the patients according to the age (< 65 vs ≥ 65 years). We found the adverse impact of the coexisting comorbidities on death is considerable in patients less than 65 years. This finding provides some evidence in that fatality of COVID-19 patients more than 65 years is independent of the presence of any comorbidity.

Strengths and limitations

To the best of our knowledge, it was the first multicenter cohort study on Iranian people with COVID-19 exploring the association between a spectrum of comorbidities and a complicated hospital course. Moreover, data on comorbidities were available for more than 90% of the admitted patients. However, this study has several limitations. First, due to the urgency of data extraction, random sampling could not be applied in our study. Second, comorbidities were self-reporting. Under-reporting of comorbidities due to the lack of awareness or diagnostic testing might confound the strength of their association with the clinical outcomes.

In this cohort of Iranian people with COVID-19, the presence of malignancy, lung disease, HF, CKD, and DM were predictors of a complicated hospital course. DM and CKD were also risk factors of in-hospital mortality. Moreover, there is an incremental risk of in-patient mortality with increased burden of comorbidity in hospitalized patients less than 65 years old.

Declarations

Acknowledgements We really appreciate the hospital staff for their efforts in collecting the information. We also thank the staff working in the Institute of Endocrinology and Metabolism for their efforts in data entry and verification.

Authors' contributions

NT and MEK contributed to the design of work. ZE, RA, MH and FA contributed to the acquisitions and analysis of the data. NHM, MM and MEK contributed to the interpretation of the data. AKh cleaned and analyzed data. NT, NHM and MEK drafted the work or substantially contributed to revising it. All authors read and approve the manuscript.

Funding

No fund.

Availability of data and materials

Datasets used in the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All methods were carried out in accordance with Declaration of Helsinki. The study was approved by the ethics committee of the Iran University of Medical Sciences. The need of informed consent was waived by ethical committee of Iran University of Medical Sciences.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–9.
2. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–62.
3. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. *Diabetes Metab Syndr*. 2020;14(4):303–10.
4. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, et al. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med*. 2020;201(11):1380–8.
5. Sepandi M, Taghdir M, Alimohamadi Y, Afrashteh S, Hosamirudsari H. Factors associated with mortality in COVID-19 patients: a systematic review and meta-analysis. *Iran J Public health*. 2020;49(7):1211.
6. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, et al. Comorbidity and its impact on patients with COVID-19. *SN Compr Clin Med*. 2020;2:1069–1076.
7. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging*. 2020;12(7):6049.
8. Roncon L, Zuin M, Zuliani G, Rigatelli G. Patients with arterial hypertension and COVID-19 are at higher risk of ICU admission. *Br J Anaesth*. 2020;125(2):e254-e5.
9. Jain V, Yuan J-M. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. *Int J Public health*. 2020;65:533–46.
10. Arthur M. Institute for health metrics and evaluation. *Nursing Standard*. 2014;28(42):32.
11. Chen Z, Peto R, Zhou M, Iona A, Smith M, Yang L, et al. Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. *Lancet*. 2015;386(10002):1447–56.
12. Raoofi A, Takian A, Sari AA, Olyaeemanesh A, Haghighi H, Aarabi M. COVID-19 pandemic and comparative health policy learning in Iran. *Arch Iran Med*. 2020;23(4):220–34.
13. Bevan JS, Adams CB, Burke CW, Morton KE, Molyneux AJ, Moore RA, et al. Factors in the outcome of transsphenoidal surgery for prolactinoma and non-functioning pituitary tumour, including pre-operative bromocriptine therapy. *Clin Endocrinol*. 1987;26(5):541–56.
14. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. *J Clin Virol*. 2020;127:104378.
15. Mounesan L, Eybpoosh S, Haghdooost A, Moradi G, Mostafavi E. Is reporting many cases of COVID-19 in Iran due to strength or weakness of Iran's health system? *Iran J Microbiol*. 2020;12(2):73–76.
16. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. *Stata Journal*. 2013;13(3):492–509.
17. Guan W-j, Liang W-h, Zhao Y, Liang H-r, Chen Z-s, Li Y-m, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020;55(5): 2000547.
18. Baradaran A, Ebrahimzadeh MH, Baradaran A, Kachooei AR. Prevalence of comorbidities in COVID-19 patients: a systematic review and meta-analysis. *Arch Bone Jt Surg*. 2020;8(Suppl 1):247–255.
19. Hu Y, Sun J, Dai Z, Deng H, Li X, Huang Q, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. *J Clin Virol*. 2020;127:104371.
20. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol*. 2020;52(6):1193–1194.
21. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in COVID-19. *N Engl J Med*. 2020;382(26):2582.
22. Guo L, Shi Z, Zhang Y, Wang C, Moreira NCDV, Zuo H, et al. Comorbid diabetes and the risk of disease severity or death among 8807 COVID-19 patients in China: a meta-analysis. *Diabetes Res clin Pract*. 2020;166:108346.

23. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr.* 2020;14(4):535–545.
24. Zhu L, She Z-G, Cheng X, Qin J-J, Zhang X-J, Cai J, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. *Cell Metab.* 2020.
25. Palaiodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, et al. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. *Metabolism.* 2020;108:154262.
26. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int.* 2020;97(5):829–838.
27. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA.* 2020;323(20):2052–2059.

Figures

Figure 1

Kaplan-Meier survival curve categorized by the number of comorbidities.

Figure 2

Predictors of death in the proportional hazard models. Hazard ratios (95% confidence interval) are shown for the comorbidities associated with the death during the hospital course. The comorbidities were classified according to the type and the number. The scale bar indicates the hazard ratio. Data were adjusted for age, sex, and the other comorbidities. DM; Diabetes mellitus, HTN; Hypertension, CAD; Coronary artery disease, HF; Heart failure, CVA; Cerebrovascular accident, CKD; Chronic kidney disease.

Figure 3

Predictors of death in the proportional hazard models stratified by the age. Hazard ratios (95% confidence interval) are shown for the comorbidities associated with the death during the hospital course. The comorbidities were classified according to the type and the number stratified by the age. The scale bar indicates the hazard ratio. Data were adjusted for age, sex, and the other comorbidities. DM; Diabetes mellitus, HTN; Hypertension, CAD; Coronary artery disease, HF; Heart failure, CVA; Cerebrovascular accident, CKD; Chronic kidney disease.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFig1.jpg](#)