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Characteristics and Recovery Prognosis Factors Among COVID-2019 Infected Cases: A Tunisian Nationwide Analysis

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Research article

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Abstract

Background: The outbreak of coronavirus disease (COVID-19) continues to constitute a public health of international concern. Few data are available on the duration and prognosis factors for recovery. We aimed to study the recovery time among a Tunisian cohort of COVID-19 confirmed patients and identify its prognosis factors.

Methods: A retrospective and national study was conducted from March 2 to May 8, 2020, recruiting all patients who were diagnosed with COVID-19, by RT-PCR methods, in Tunisia. Data were collected via phone call interview. Kaplan-Meir Methods and Cox proportional hazards regression models were, respectively, used to study the recovery time and estimate its prognosis factors.

Results: 1030 patients with COVID-19 (aged 43.2 ± 18.2 years, 526 female (51.1%)) were enrolled. Among them 174 (16.9%) were healthcare professionals. Out of 173 patients (17.8%) admitted to the hospital, 47 were admitted in an intensive care unit. Among those who didn't require specialized care, 55.5% were self-isolated at home, while the rest were in specialized centers. Almost ¾ of the patients were symptomatic. A total of 634 (61.6 %) patients have recovered and 45 (4.4 %) patients died. The median duration of illness was estimated to be 31 days (95% CI: [29 - 32]). Older age (HR=0.66, CI:[0.46-0.96], P=0.031) and symptoms (HR=0.61, CI:[0.43-0.81], P=0.021) were independently associated with a delay in recovery time. Being a healthcare professional (HR=1.52, CI :[1.10-2.08], P=0.011) and patients in home isolation compared to isolation centers (HR=2.99, CI :[1.85-4.83], $P<10^{-3}$) were independently associated with faster recovery time.

Conclusion: the duration of illness was estimated to be one month. However, this long estimated duration of illness may not equate to infectiousness. A particular attention must to be paid to elderly and symptomatic patients with closer monitoring.

Background

Coronavirus disease 2019 (COVID-19), an infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was first reported in December 2019, in Wuhan, Hubei Province in China. Since then, the number of cases increased rapidly in China and soared dramatically across the world with human-to-human transmission to become one of the most challenging global health problems. On 30 January 2020, the World health organization considered COVID-19 as a public health emergency of international concern and announced the pandemic threat in March 11,2020 (1, 2). On May 15, 2020, 4 553 394 confirmed cases of covid-19 were identified, worldwide, with death rate of 6.7% and 37.7% of recovery(3) .

In Tunisia, the first confirmed case of COVID-19 was reported on March 2, 2020. Since then, several measures have been taken to brake the spread of the epidemic among the population, including successively screening at point of entry, 14 days isolation of travelers returning from risk areas, closure of school and university facilities, ban of sports and cultural events, borders closure, curfew and finally, a

national lockdown was announced on March 22, 2020. On May 8, 2020, the total number of confirmed cases of COVID-19 was 1030 (4).

Several studies have addressed clinical, radiological and biological issues in COVID-19 patients. The clinical spectrum is large and ranges from asymptomatic or mild forms, accounting for about 80%, to cases of acute respiratory distress syndrome that may lead to intensive care or death(5).

However, we note a scarcity of data on prognosis factors associated with a better outcome and recovery. Since an early recovery reduces the shedding and spread of the virus, identifying recovery prognosis factors may improve our understanding of the dynamics of transmission and foster the control of the epidemic (6).

The present study aims to estimate recovery time and identify related prognosis factors among Tunisian infected people with COVID-19.

Methods

Study design

Our study includes all confirmed COVID 19 cases listed among the database of the national observatory of new and emerging diseases (ONMNE), which is the national center for disease control and surveillance.

Case definition

A confirmed COVID-19 case is defined as any person, whether symptomatic or not, with laboratory confirmation of SARS-CoV-2 infection using real-time reverse transcriptase–polymerase chain reaction (RT-PCR).

Laboratory confirmation of SARS-CoV-2 infection

The laboratory testing for SARS by RT/PCR was the laboratory method of reference to confirm cases. Charles Nicolle hospital laboratory which is the national influenzae World Health Organisation (WHO) collaborating laboratory was the reference laboratory at national level. It received all the specimens during the first period of outbreak investigation. Later on, other laboratories performing SARS specific PCR tests were invloved.

SARS-CoV-2 infection was confirmed in all patients by testing nasopharyngeal swab samples with a real-time reverse transcription– polymerase chain reaction assay

Recovery monitoring and criteria

From March 2, 2020, when the first case was reported, all confirmed cases are consistently and timely reported by the laboratory to the national observatory for new and emerging diseases (ONMNE) where a team of trained physicians was responsible to ensure the follow-up of all confirmed cases by phone calls.

All positive cases are assigned to keep a 14 days quarantine until to get two negative laboratory testing. Epidemiological, demographic, isolation setting and conditions, symptoms, treatment and outcome data were collected from positive cases during the quarantine. COVID-19 patients were isolated at home or in dedicated covid-19 centers. Hospitalization was only indicated for the serious cases requiring a respiratory assistance or special care. The recovery statement is based on laboratory data. For asymptomatic patients, the first recovery testing is scheduled for the last day of the quarantine. For symptomatic patients, the first recovery testing is done three days after the symptoms disappearance and at least seven days after onset symptoms. In both situation, the second recovery testing is done 24 to 48 h after the first negative sample. If the first recovery test is still positive, then the second recovery test is done 7 days later. The formal recovery criteria is defined by two successive negative RT-PCR control specimen and recovery time is defined as the period from the date of symptoms onset to the date of second negative RT-PCR test result (when patients got positive RT-PCR result following false negative result, it was considered as non-effective negative result in our study). After recovery statement, a mandatory 14 days home auto-isolation is indicated.

Statistical analysis

Statistical analysis were performed using SPSS version 17.0 software. Data were expressed as frequencies and percentages for categorical variables and as means and standard deviations (SD) or medians and interquartile ranges (IQR) as appropriate for continuous variables. The median time to recovery was estimated by Kaplan-Meir Methods. Cox proportional hazards regression models were used to estimate factors influencing the recovery time, with the hazards ratio (HR) and its 95% confidence interval (95%CI). Statistical significance was determined at $P < 0.05$.

Results

Clinical profile of patients

A total of 1030 patients tested positive for COVID 19 disease were collected between March 2 and Mai 8, 2020. The mean age was 43.2 years ± 18.2, and 526 (51.1%) were female. Almost all patients are Tunisians (Table 1) and quarter of infections were imported, mainly from France or Turkey. One hundred seventy three patients (17.8%) were admitted to the hospital, most of them in a non-intensive care department and only 47 in an intensive care unit (ICU). Sixty six patients (38%) received an hydroxy-chloroquine treatment. Half of the cases received such treatment in a hospital setting and the others received it either from a private doctor or as self-medication. Patients who do not require care have been self-isolated at home (55.5%) or in dedicated centers for positive cases (44.5%). One hundred forty one patients were healthcare professionals who were infected in half of the cases in a healthcare setting.

Table 1
Demographic and clinical characteristics of patients with COVID-19 in Tunisia.

Characteristics	N (%)
Age groups (years)	
< 15	63 (6.3)
15–34	287 (28.9)
35–54	369 (37.2)
55–74	232 (23.4)
≥ 75	42 (4.2)
Gender	
Male	504 (48.9)
Female	526 (51.1)
Nationality	
Tunisian	999 (97)
Non Tunisian	31 (3)
Medical staff	
Yes	141 (14.8)
No	809 (85.2)
Contamination mode	
Imported contamination	246 (23.9)
Local contamination	783 (76.1)
Hospitalization	
Yes	173 (17.8)
No	800 (82.2)
Admission to ICU	
Yes	47 (4.8)
No	926 (95.2)
Isolation mode	

ICU: intensive care unit

Characteristics	N (%)
Home isolation	459 (55.5)
Isolation center	368 (44.5)
Symptoms	
Yes	602 (74.7)
No	204 (25.3)
Chloroquine treatment	
Yes	66 (7.8)
No	779 (92.2)
ICU: intensive care unit	

Almost 75% of patients had symptoms. The most common symptoms were fatigue, cough and fever, which occurred respectively in 51.6%, 51.3% and 48.3% of symptomatic patients. Symptoms such as headache, anosmia and digestive signs were also common in those patients (Table 2).

Table 2
Distribution of clinical signs among symptomatic patients with COVID-19 in Tunisia.

Symptoms	N = 602
Cough	311 (51.6)
Fatigue	309 (51.3)
Fever	291 (48.3)
Headache	210 (34.8)
Anosmia	195 (32.4)
Digestive signs	188 (31.2)
Loss of taste	165 (27.4)
Dyspnea	140 (23.3)
Others signs	129 (21.4)

As of May 8, 2020, a total of 634 (61.6%) patients were recovered, 45 (4.4%) patients were dead and 351 (34%) were still being followed.

Recovery prognosis factors

Survival analysis was used to analyze the prognosis factors for recovery in patients with COVID-19. It showed that the median duration of illness was estimated to be 31 days (95%Confidence Interval [CI]: [29–32])(Fig. 1). In univariate analysis, older age (Fig. 2), imported transmission of the infection and being symptomatic (Fig. 3) were associated with a longer duration of illness. Whereas, being a healthcare worker (Fig. 4) and patients in home isolation (Fig. 5) were associated with a shorter duration of illness. Using Cox regression, older age (HR = 0.66, CI:[0.46–0.96], P = 0.031) and having symptoms (HR = 0.61, CI:[0.43–0.81], P = 0.021) were independently associated with a delay in recovery time. Being a healthcare professional (HR = 1.52, CI :[1.10–2.08], P = 0.011) and patients in home isolation compared to isolation centers (HR = 2.99, CI :[1.85–4.83], P < 10^{-3}) were independently associated with faster recovery time (Table 3).

Table 3
factors associated with recovery time among patients with COVID-19 in Tunisia.

	Univariate Cox regression			Multivariate Cox regression		
	HR	95% CI	P value	HR	95% CI	P value
Male	0.93	0.79–1.09	0.405			
Age > 60 years	0.68	0.55–0.85	0.001	0.66	0.46–0.96	0.031
Tunisian Nationality	0.93	0.57–1.50	0.754			
Healthcare worker	1.86	1.52–2.27	< 10^{-3}	1.52	1.10–2.08	0.011
Imported infection	0.83	0.69–0.99	0.038			
Home isolation	1.69	1.4–2.06	< 10^{-3}	2.99	1.85–4.83	< 10^{-3}
Hospitalization	0.95	0.76–1.18	0.635			
Admission in ICU	0.95	0.71–1.28	0.73			
Symptoms	0.56	0.46–0.68	< 10^{-3}	0.61	0.43–0.81	0.001
Chloroquine treatment	1.09	0.82–1.46	0.55			

Discussion

Several studies have described the epidemiological, clinical, and radiological profile of patients with confirmed COVID-19 infection (7, 8) but few studies have focused on the course including the recovery issue and how much time that needs of the disease.

We described the demographic and clinical characteristics of confirmed COVID-19 Tunisians patients, estimated the median disease duration using the survival analysis and investigated the factors affecting the recovery time for COVID-19.

The main result of our study is the long duration of the disease. The patient is announced cured 31 days from the first day of the onset of symptoms for symptomatic patients and from the laboratory confirmation date for the asymptomatic patients.

Our national cohort reached 1,030 COVID-19 infected patients. It is a relatively young population with almost patients under 55 years of age. In the literature, a mean age between 48 and 55 years was reported (7, 9–12). For the gender, there was no predominance of men or women. The number of imported cases was higher than the number of local contaminations until 03/18/2020. The trend reversal (local contamination vs imported cases) was evident from 03/21/2020 announcing the installation of horizontal transmission (13).

Most of cases were mild as evidenced by relatively low ICU admissions and a high number of asymptomatic patients or with mild symptoms that do not require treatment in a hospital structure. In fact, the proportion of mild and asymptomatic cases versus severe and fatal cases for COVID-19 infection is currently still unknown. According to a Chinese report publishing all confirmed, suspected, and asymptomatic cases in China, 80% of infections were mild and can recover at home (14). Concerning clinical presentation of COVID-19 disease, the common symptoms reported by symptomatic patients were cough, fatigue and fever in nearly half of cases and headache in 35% of cases, which was consistent with general symptoms of viral infection. Similar symptoms were described in several case series (7, 10, 15). One out of three symptomatic patients reported loss of smell and/or taste. This type of disturbance was widely reported in the literature specially among patients with mild and moderate forms of coronavirus disease (16, 17).A multicenter European study showed that 85.6% and 88.0% of patients reported olfactory and gustatory dysfunctions (18).

The median duration of illness was estimated to be 31 days counting from the day of onset symptoms for symptomatic patients and from confirmation date for asymptomatic patients. This estimation for illness duration was long. In a recent Singapore study, similar results were recorded. It indicate that by day 15 from onset of illness, only 30% of all COVID-19 patients are PCR-negative by nasopharyngeal swab, this rises to 95% by day 33 (19). According to these results, the duration of viral shedding by PCR may extend to a month and sometimes longer for a small group of patients. Current guideline suggested two consecutive negative RT-PCR test results is one of the criteria for hospital discharge or discontinuation of quarantine. However, a high false negative rate of viral test was reported(20) and some patients experienced a “turn positive” of nucleic acid detection by RT-PCR test for SARS-CoV-2 after two consecutive negative results, which may be related to the false negative of RT-PCR test and prolonged nucleic acid conversion (21). The Singapore study indicates also that viable virus was not found after the second week of illness despite the persistence of PCR detection of RNA(19). It is, then, important to note that traces of virus detected by RT-PCR were not necessarily correlated with the ability of transmission.

In addition, a recent Canadian study demonstrate that infectivity as defined by growth cell culture were most likely between days one and five (22). These data indicate that even viral RNA detection may persist

in some patients, such persistent RNA detection represent non-viable virus and such patients are non-infectious(19). These findings are consistent with the new WHO recommendations for discontinue transmission-based precautions (including isolation) and release from the COVID-19 care pathway (23) with 10 days after symptom onset, plus at least 3 days without symptoms for symptomatic patients and 10 days after test positive for asymptomatic patients. These new recommendations should be taken in a count to adapt strategy to discontinue isolation of COVID-19 patients in our country.

Cox regression model showed that younger patients recover faster compared to elderly patients. Similar findings were reported (24, 25). In fact, many studies found a high proportion of severe cases and fatality rate among elderly patients with COVID-19 (11, 26–29).

Based on the result of this study, being a healthcare worker was showed to be significantly associated to a lower median time to viral clearance after onset of symptoms. This finding could be explained by the fact that the healthcare workers' monitoring and control protocol is different from that of other COVID-19 patients. Indeed, the COVID-19 monitoring and control protocol adopted by the Tunisian health authorities was inspired from the recovery criteria of the European center for disease prevention and control (ECDC) documents (30). This protocol consists in carrying out a control sample for asymptomatic patients after 14 days from the date of confirmation. For symptomatic ones, if the fever or any other signs persist beyond 14 days, the control sample will be postponed for 3 days after the disappearance of the last sign. These deadlines are not respected for healthcare staff involved in the clinical management of COVID-19 patients. Healthcare workers infected with COVID-19 follow a closer control protocol, which may explain the faster time to viral clearance among them.

Results showed that the place of isolation is playing a significant role in survival time to recovery from COVID-19 infection. According to the output of the cox model, COVID-19 patients in self-isolation at home are almost three times more likely to recover faster than those in dedicated COVID-19 centers. In fact, the Tunisian strategy was based in the first phase of the epidemic on the isolation of confirmed COVID-19 cases in their place of residence and to hospitalize only the serious cases requiring a respiratory assistance or special care. Afterwards, given the registration of an increasing number of secondary cases among the close contacts of confirmed patients, the health authorities decided to create specialized centers to isolate COVID-19 patients in order to limit community transmission. The delay in recovery for COVID-19 patients isolated in COVID-19 centers compared to those in self-isolation at home could be explained by the fact that patients do not respect self-isolation inside these centers leading sometimes to mass gatherings. This promiscuity inside the dedicated centers for infected people may thus promote the maintenance of viral load.

Symptomatic patients seem also to have slower recovery duration.

This study has some limitations. There was a lack in some clinical information such as comorbidities and vital signs (heart rate, respiration rate, blood pressure….). In addition, since we used phone interview information concerning, biological and radiological data were not available for patients who have been hospitalized.

Conclusions

The study findings showed that the estimated duration of illness was excessively long, which influenced Tunisian jurisdictions to guide policies of firm isolation and discharge. This partly explains the success in controlling the epidemic in Tunisia. However, with current science data, which proves that viral detection by PCR does not equate to infectiousness, we strongly recommend to lighten our quarantine strategy in accordance with the new WHO recommendations.

We also found that older age and symptoms were independently associated with slower recovery time, whereas healthcare professional and patients in self-isolation at home were independently associated with faster recovery time. These results reinforce guidance that additional control measures must be undertaken to avoid mass gatherings inside isolation centers. Elderly and symptomatic patients need particular attention and closer monitoring.

Abbreviations

COVID-19: Coronavirus disease, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, WHO: World Health Organization, ONMNE: The National Observatory of New and Emerging Diseases, RT-PCR: Real-time reverse transcriptase–polymerase chain reaction, SARS: Severe acute respiratory syndrome, ECDC: The European center for disease prevention and control.

Declarations

Ethics approval and consent to participate

The follow-up data of individual patients were collected via National Observatory of New and Emerging Diseases of Tunis, Tunisia. Data were anonymized for this study. Neither ethical approval nor individual consent was not applicable.

Consent for publication

Not applicable.

Availabilityof data and materials

All data supporting our findings are contained within this article

Competing interests

None declared.

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Authors' contributions

CH interpreted the data and drafted the manuscript. IC, NN, MO, RM, OB, YA and IB collected the data and performed the literature research. AH, MS and HL provided helpful information. MKC and NBB designed the study, provided guidance and approved the final manuscript. All authors discussed the results, critically read and revised the manuscript and gave final approval for publication.

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References

1. 1. Organization WH. WHO announces COVID-19 outbreak a pandemic 2020 [2020 May 13]. Available from: http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic.
2. 2. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020 Apr;76:71 – 6. PubMed PMID: 32112977. Pubmed Central PMCID: 7105032.
3. 3. Coronavirus Outbreak [15 may 2020]. Available from: : https://www.worldometers.
4. info/coronavirus/.
5. 4. COVID-19-dernier-bulletin.pdf [2020 May 14]. Available from: http://www.onmne.tn/fr/images/COVID-19-dernier-bulletin.pdf.
6. 5. Yang X, Yu Y, Xu J, Shu H, Xia Ja, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020;8(5):475 – 81.
7. 6. Wölfel R CV, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. virological assessment of hospitalized patients with COVID-2019. Nature. 2020:1 – 5.
8. 7. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507 – 13.
9. 8. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. Jama. 2020 Mar 3. PubMed PMID: 32125362. Pubmed Central PMCID: 7054855.
10. 9. Choi WS, Kang CI, Kim Y, Choi JP, Joh JS, Shin HS, et al. Clinical Presentation and Outcomes of Middle East Respiratory Syndrome in the Republic of Korea. Infection & chemotherapy. 2016

Jun;48(2):118 – 26. PubMed PMID: 27433382. Pubmed Central PMCID: 4945721.

11. 10. Singhal T. A Review of Coronavirus Disease-2019 (COVID-19). Indian journal of pediatrics. 2020 Apr;87(4):281-6. PubMed PMID: 32166607. Pubmed Central PMCID: 7090728.
12. 11. Zhao X, Zhang B, Li P, Ma C, Gu J, Hou P, et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis. MedRxiv. 2020.
13. 12. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. The European respiratory journal. 2020 May;55(5). PubMed PMID: 32217650.
14. 13. Decree 98-2248 of November 16, 1998, fixing public places in which smoking is banned., n°94.24 November 1998 : 04.
15. 14. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama. 2020;323(13):1239-42.
16. 15. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020 Feb 19;368:m606. PubMed PMID: 32075786. Pubmed Central PMCID: 7224340 at and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
17. 16. Andrea Giacomelli LP, Federico Conti, Dario Bernacchia, Matteo Siano, Letizia Oreni and al. Self-reported Olfactory and Taste Disorders in Patients With Severe Acute Respiratory Coronavirus 2 Infection:
18. A Cross-sectional Study. Clin Infect Dis. 2020;DOI: 10.1093/cid/ciaa330.
19. 17. Lee Y, Min P, Lee S, Kim SW. Prevalence and Duration of Acute Loss of Smell or Taste in COVID-19 Patients. Journal of Korean medical science. 2020;35(18):e174.
20. 18. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies. 2020 Apr 6. PubMed PMID: 32253535. Pubmed Central PMCID: 7134551.
21. 19. The National Centre for Infectious Diseases and the Chapter of Infectious Disease Physicians AoM. Period of Infectivity to Inform Strategies for De-isolation for COVID-19 Patients. Singapore: 2020 23 May 2020. Report No.
22. 20. Li Y, Yao L, Li J, Chen L, Song Y, Cai Z, et al. Stability issues of RT-PCR testing of SARS-CoV-2 for hospitalized patients clinically diagnosed with COVID-19. Journal of medical virology. 2020 Mar 26. PubMed PMID: 32219885. Pubmed Central PMCID: 7228231.
23. 21. Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. Journal of medical virology. 2020 Apr 9. PubMed PMID:

32270882.
24. 22. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. Clin Infect Dis. 2020 May 22. PubMed PMID: 32442256.
25. 23. Organization WH. Clinical management of severe acute
26. respiratory infection (SARI) when COVID-19 disease is suspected. 2020 13 March 2020. Report No.
27. 24. Mollazehi M, Mollazehi M, Abdel-Salam A-SG. Modeling Survival Time to Recovery from COVID-
28. 19. : A Case Study on Singapore. BMC Public Health. 2020.
29. 25. Kaijin Xu YC, Jing Yuan, Ping Yi, Cheng Ding, Wenrui Wu and al. Factors Associated With Prolonged Viral RNA Shedding in Patients With COVID-19. Clin Infect Dis. 2020;ciaa351.
30. 26. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. Journal of Infection. 2020.
31. 27. 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. The Lancet. 2020;395(10229):1054-62.
32. 28. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus Disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. Journal of Infection. 2020.
33. 29. Rachel E Jordan PA, K K Cheng. Covid-19: risk factors for severe disease and death. BMJ. 2020;m1198
34. 30. (ECDC) TECfDpaC. Novel Coronavirus (SARS-COV-2): Discharge criteria for confirmed COVID-19-cases. ECDC Technical Report. 2020.

Figures

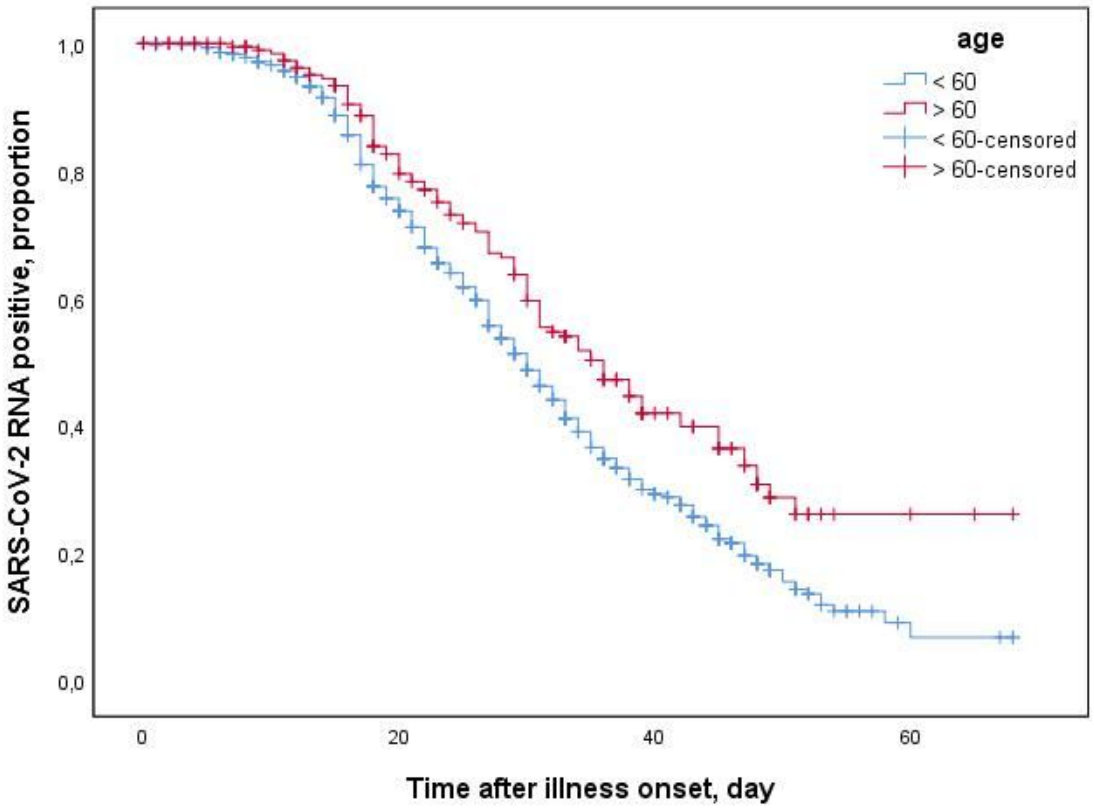

Figure 1

Survival curve showing survival time to recovery from COVID-19 infection

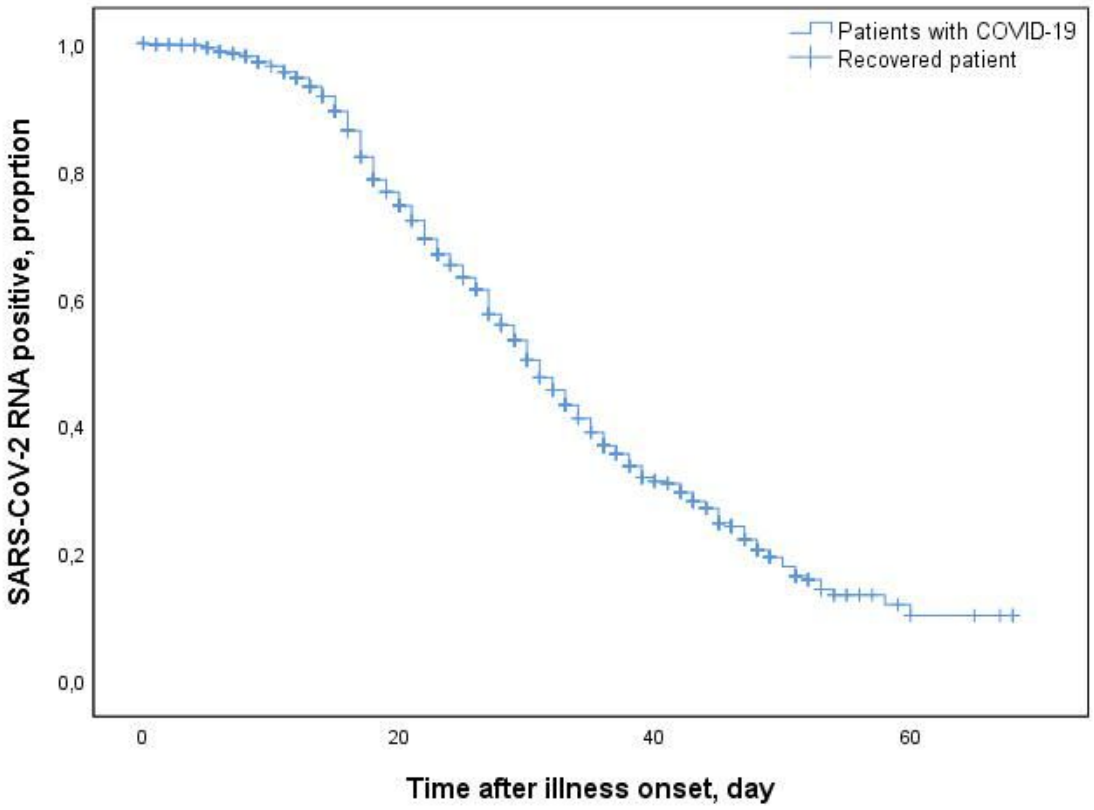

Figure 2

Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between patients aged 60 years and over and patients under 60 years.

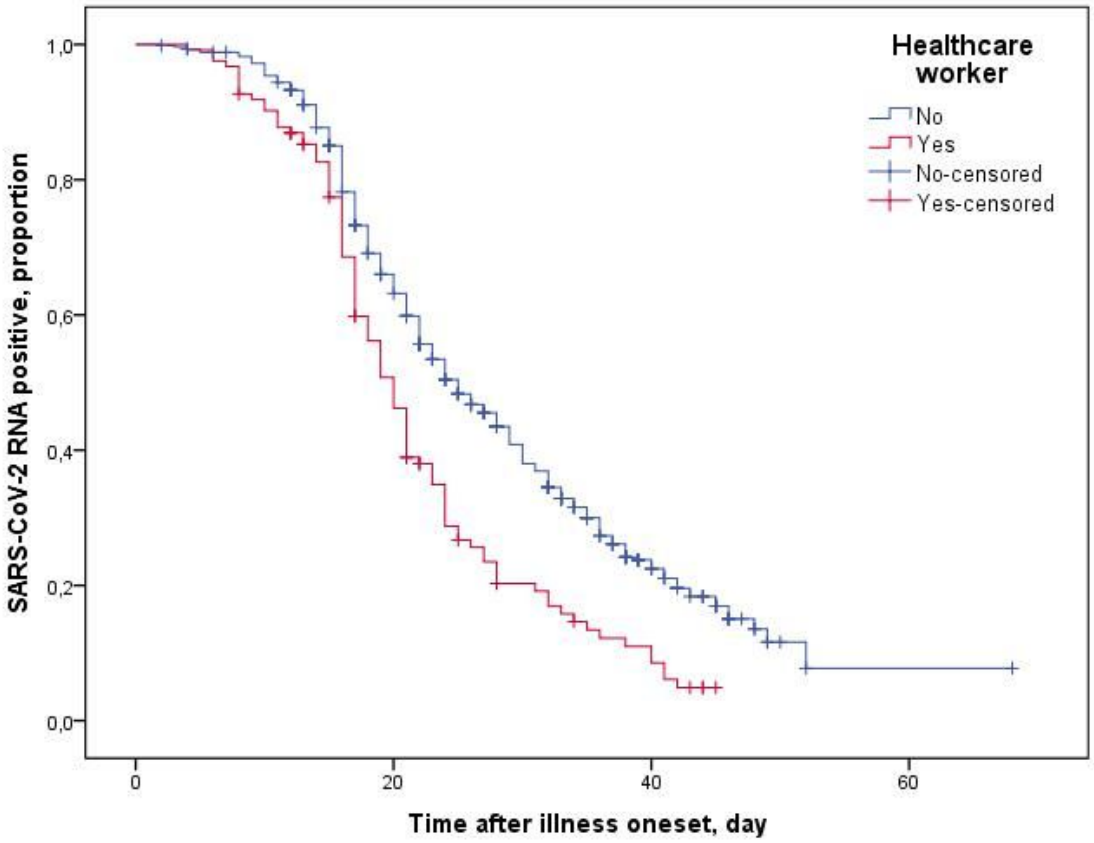

Figure 3

Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between symptomatic and asymptomatic patients.

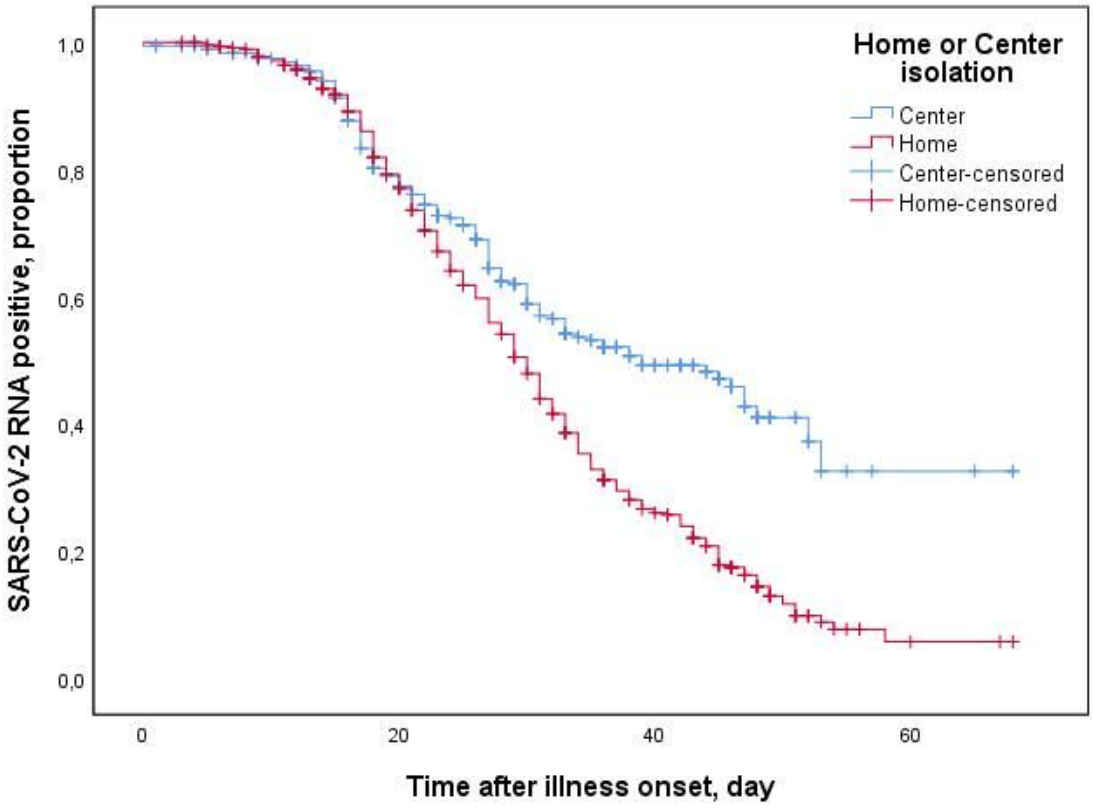

Figure 4

Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between healthcare worker and other patients.

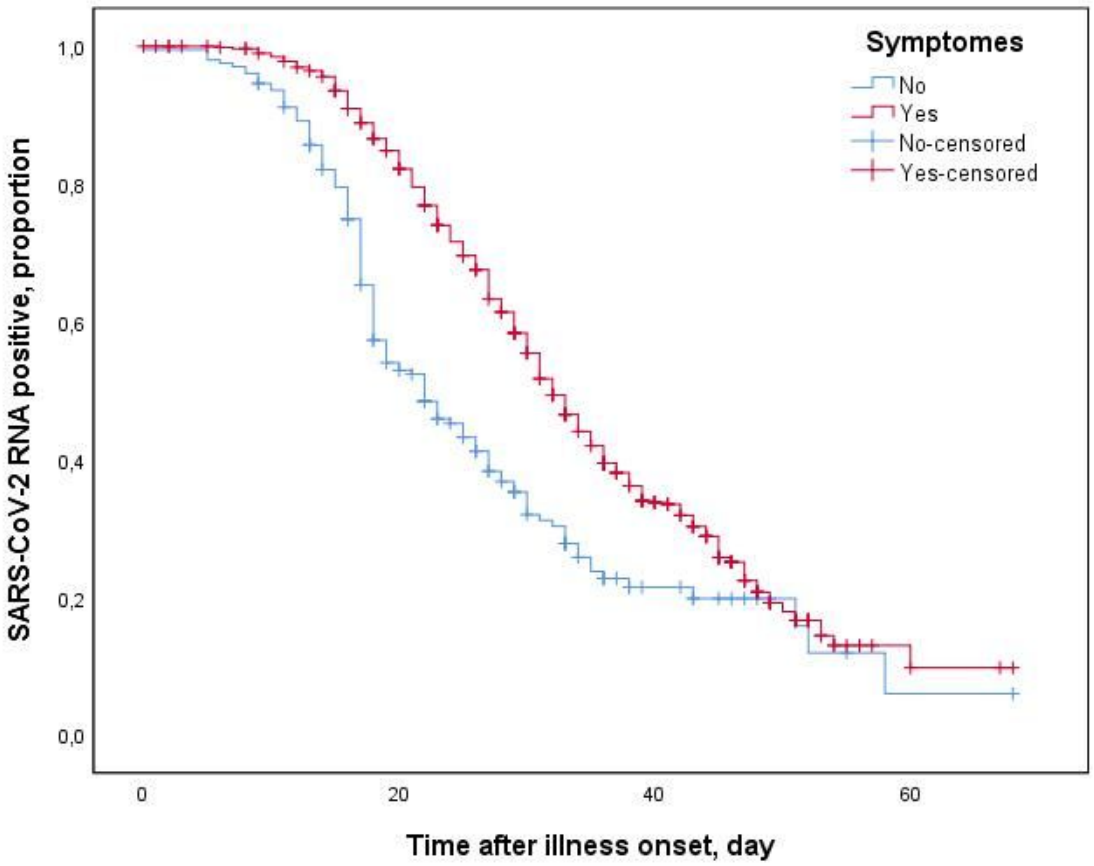

Figure 5

Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between patients in home isolation and patient in dedicated centers for positive cases.