Health-related quality of life of COVID-19 survivors at 6 months after hospital discharge: a cohort study

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Abstract

Background: COVID-19 is a multi-systemic disease that is highly contagious and pathogenic. The long-term consequences of it are not yet clear, as is whether society and life can return to a healthy state. Long-term assessment of their health-related quality of life (HRQoL) is essential. This study aimed to investigate HRQoL and its risk factors in COVID-19 survivors at a follow-up of 6-month.

Methods: A multicenter cross-sectional survey was conducted among 192 COVID-19 patients with confirmed age ≥ 18 years who were discharged from various hospitals in Wuhan from January to April 2020. The demographic characteristics, clinical characteristics, and laboratory results of the study subjects were obtained from the hospital's medical records. Survivors' HRQoL was assessed using the Short Form 36 (SF-36), cognition was assessed using the ascertain dementia eight-item informant questionnaire (AD8), and survivors' pulmonary function were examined. All participants in this study completed the survey and testing at Hubei Provincial Hospital of Chinese and Western Medicine. SF-36 scores were compared with the Chinese norm, and logistic regression and multivariate analysis were used to investigate the factors affecting HRQoL in COVID-19 survivors. Results: SF-36 showed significant differences in HRQoL between COVID-19 survivors and the general Chinese population (P< 0.05). Multiple linear regression demonstrated that age was negatively correlated with physical functioning (PF), role-physical limitation (RP) and social functioning (SF) (P <0.05). Bodily pain (BP), vitality (VT), SF and role-emotional limitation (RE) were negatively correlated with females (P <0.05). Length from discharge to follow-up was positively correlated with PF and RP (P <0.05). Abnormal cognitive function was negatively correlated with PF, RP, general health (GH), VT, SF, RE and mental health (MH) (P <0.05). Abnormal Carbon Monoxide Diffusing Capacity (DLCO%<80%) was significantly negatively correlated with PF and SF (P <0.05). In addition, there was a significant negative correlation between Coronary heart disease and RP, GH, VT and RE (P <0.05). Logistic regression analysis demonstrated that age(OR 1.032) and AD8 scores (OR 1.203) were risk factors associated with a low physical component summary (PCS) score. Length from discharge to follow-up (OR 0.971) was the protective factor for PCS score. Abnormal cognitive function (OR 1.543) was a significant determinant associated with a mental component summary (MCS)<50 in COVID-19 patients. Conclusions: The HRQoL of COVID-19 survivors remains to be improved at six-month follow-up. Future studies should track HRQoL in older adults, women, patients with abnormal DLCO, and abnormal cognitive function for a long time and provide them with rehabilitation advice and guidance.

Background

In January 2020, Chinese scientists identified a novel coronavirus, 2019-nCoV, which revealed the culprit of this infectious viral pneumonia that has attracted much attention in the world[1]. COVID-19 is highly infectious and pathogenic, and as of November 19, 2020, it has caused 1,333,742 deaths worldwide[2]. Some COVID-19 patients will experience lung injury, brain microstructural changes, olfactory and taste dysfunction, alopecia and psychosocial damage after rehabilitation and discharge[3-5].

Health-related quality of life(HRQoL) is a multidimensional concept influenced by economic and social factors, life satisfaction, and the severity and stage of a disease[6, 7]. Studies have reported that COVID-19 survivors have decreased health-related quality of life at one-month follow-up[8, 9], but it is unknown whether COVID-19 has a longer-term effect on HRQoL. Long-term assessment of health-related quality of life in COVID-19 survivors is essential in order to develop strategies and interventions to improve their quality of life. Therefore, this study aimed to investigate HRQOL and its risk factors in COVID-19 survivors at six months after rehabilitation.

Methods

Study Design and Participants

Patients were recruited from September to October 2020 at the Physical Examination Center of Hubei Provincial Hospital of Chinese and Western Medicine after the eligibility evaluation. The study protocol followed the ethical principles of the Declaration of Helsinki and was approved by the Ethics Committee of Guangdong Provincial Hospital of Traditional Chinese Medicine (No. BF2020-205-01). All patients signed an informed consent.
The target subjects of this cross-sectional study were COVID-19 confirmed patients, aged ≥ 18 years, discharged from January – April 2020 in Wuhan, Hubei Province, China. The diagnosis was based on the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) published in China[10]. A COVID-19 patient was identified through the SARS-CoV-2 virus infection by RT-PCR, viral gene sequencing or serum anti-SARS-CoV-2 IgM detection. The severity of COVID-19 infection was divided into mild, the clinical symptoms were mild, and there was no sign of pneumonia on imaging; moderate, showing fever and respiratory symptoms with radiological findings of pneumonia; severe, adult cases meeting any of the following criteria: respiratory distress ≥ 30 breaths/ min; oxygen saturation ≤ 93% at rest; arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) ≤ 300 mmHg (1 mmHg = 0.133 kPa); and critical, cases meeting any of the following criteria: respiratory failure and requiring mechanical ventilation; shock; with other organ failure that requires ICU care.

According to their wishes, 192 participants completed demographic and medical history data collection, SF-36 questionnaire, AD8 questionnaire and pulmonary function examination.

**Questionnaires and Laboratory Tests**

Demographic characteristics, co-morbidities, Clinical subtype of 192 subjects were obtained from their medical records. All participants in this study completed questionnaires and laboratory tests at Hubei Provincial Hospital of Chinese and Western Medicine. Questionnaires and laboratory tests are as follows:

1. Health-related quality of life (HRQoL) was evaluated using the SF-36 translated into Chinese, which is a common evaluation method for HRQoL [11]. The measure consists of a health transition (HT) single item and 35 other items that are assessed in eight item categories: physical functioning, role-physical limitation, bodily pain, general health, vitality, social functioning, role-emotional limitation, and mental health with scores from 0 to 100, with 0 representing the most unfavorable functional status and 100 representing the most favorable functional status. Physical component summary score (PCS) and mental component summary score (MCS) were calculated using z-transformed scores as well as factor score coefficients, with low MCS or PCS (< 50) indicating poor HRQoL[12].

2. Ascertain Dementia 8-item Questionnaire (AD8) is one of the fast, simple, and sensitive screening methods for detecting both minor and major cognitive impairments[13]. AD8 consists of a series of 8 statements, which are classified as "yes", "no", or "don't know" by the patient or informant, and the total score is given by the sum of the answers "yes" (range: 0 – 8; higher scores are considered worse). Use specified boundaries (0-1: normal cognition; ≥ 2: possible cognitive impairment) [14].

3. Pulmonary function: the pulmonary ventilation function and pulmonary diffusion capacity were measured using computerized medisoft instrument (HypAir FeNO®; Medisoft, Belgium), also international recommendations[15].

**Chinese Population Norm**

The Chinese population norm was based on the study done by Wang and his colleagues who used a Mandarin version of the SF-36 to evaluate adults in mainland China through a randomly-stratified multistage sampling design[16].

**Statistical Analysis**

Data analyses were performed using the SPSS 18.0 statistical software package (SPSS Inc. IBM Corporation, Armonk, New York, USA). Categorical data were described by frequency and constituent ratio, and chi-square test and fisher's exact test were used to compare the groups. Data were expressed as mean±standard deviation or median (interquartile range) for normally and non-normally distributed data, respectively; differences in SF-36 scores among survivors with different demographic/c clinical and laboratory characteristics were analyzed by t-test, one-way ANOVA tests, or non-parametric Mann-Whitney U tests; correlations were analyzed by Pearson's or Spearman's correlation coefficients. If there were significant correlations, a stepwise multiple linear regression model was constructed to determine the factors related to the SF-36 scores among the independent variables. Multivariate analyses associated with decreased PCS scores and MCS scores were performed using logistic regression analyses, with odds ratios (ORs) as the basis for evaluating the degree of impact. P-values < 0.05 were considered statistically significant.
Results

Sample Demographic and Clinical Features

A total of 192 subjects from Hubei Provincial Hospital of Traditional Chinese and Western Medicine, Hankou Hospital of Wuhan, and Leishenshan Hospital of Wuhan were recruited. Most of the patients were moderate cases (70.83%), with Physical Component Summary (PCS) < 50 of 103 (53.65%) and Mental Component Summary (MCS) < 50 of 162 (84.38%) evaluated by SF-36. The more prevalent comorbidities were hypertension (20.31%) and diabetes (11.98%). A comparison between patients with PCS ≥ 50 and those with PCS < 50 showed statistically significant differences for age, BMI, subgroup, AD8 scores, Length from discharge to follow-up, and Coronary heart diseases. Compared with the 89 survivors in the PCS ≥ 50 group, patients in the PCS <50 group were significantly older (59.86±10.10 vs. 56.47±10.96, P=0.027) and with higher AD8 scores (3.11±2.18 vs. 2.2±2.19, P=0.005). Moreover, the PCS of mild:moderate and severe or critical cases were different. Besides, patients with MCS ≥ 50 showed lower AD8 scores compared with those with MCS < 50. These data are shown in Table 1.

**TABLE 1** | Demographic, clinical and laboratory data of all recoveries and two groups of recoveries with PCS and MCS scores of 50 as cut-off points
### Scores of SF-36 in the Study

The SF-36 mean score for eight specific dimensions was measured (FIGURE 1). In these eight dimensions, PF, RP, BP, GH, VT, SF, RE and MH subgroup scores were significantly lower in patients than the Chinese population norm (P < 0.05).

### Correlates and predictors of health-related quality of life among survivors

There was a statistical significant correlation between the eight fields of the SF-36 and the assessed variables as shown in Table 2. Multiple linear regression analysis was performed with the eight fields of SF-36 as dependent variable and age, gender, clinical subtype, length from discharge to follow-up, AD8 scores, DLCO% 80%, and co-morbidities as independent variables (Table 3). Other variables were excluded from the model as they were non-significant on univariate analysis (Table 2). Age was...
negatively correlated with PF, RP and SF ($P < 0.05$). BP, VT, SF and RE were negatively correlated with females ($P < 0.05$). Follow-up time was positively correlated with PF and RP ($P < 0.05$). AD8 score was negatively correlated with PF, RP, GH, VT, SF, RE and MH ($P < 0.05$). Pulmonary function parameters (DLCO% < 80%) were significantly negatively correlated with PF and SF ($P < 0.05$). In addition, there was a significant negative correlation between Coronary heart disease and RP, GH, VT and RE ($P < 0.05$).

**TABLE 2** Statistical Significant Correlations between the eight fields of SF-36 and Variables Evaluated.
| Variables | Correlation coefficients (R/ρ) | P-value |
|-----------|-------------------------------|---------|
| PF        |                               |         |
| Age       | -0.176                        | 0.015   |
| Length from discharge to follow-up | 0.10 | 0.013 |
| AD8 scores | -0.286 | <0.001 |
| DLCO%80%  | -0.210                        | 0.030   |
| Coronary heart disease | -0.153 | 0.034 |
| RP        |                               |         |
| Age       | -0.158                        | 0.028   |
| Length from discharge to follow-up | 0.13 | 0.002 |
| AD8 scores | -0.292 | <0.001 |
| Coronary heart disease | -0.178 | 0.013 |
| BP        |                               |         |
| GenderFemale | -0.187 | 0.009 |
| AD8 scores | -0.181 | 0.012 |
| GH        |                               |         |
| GenderFemale | -0.196 | 0.007 |
| Length from discharge to follow-up | 0.112 | 0.008 |
| AD8 scores | -0.457 | <0.001 |
| DLCO%80%  | -0.163                        | 0.025   |
| Diabetes  | -0.149                        | 0.039   |
| Coronary heart disease | -0.232 | 0.001 |
| VT        |                               |         |
| GenderFemale | -0.262 | <0.001 |
| AD8 scores | -0.374 | <0.001 |
| Coronary heart disease | -0.259 | <0.001 |
| SF        |                               |         |
| Age       | -0.155                        | 0.032   |
| GenderFemale | -0.184 | 0.011 |
| AD8 scores | -0.243 | 0.001 |
| DLCO%80%  | -0.219                        | 0.013   |
| RE        |                               |         |
| Length from discharge to follow-up | 0.114 | 0.006 |
| AD8 scores | -0.0310 | <0.001 |
| Coronary heart disease | -0.214 | 0.003 |
| MH        |                               |         |
| GenderFemale | -0.222 | 0.002 |
| AD8 scores | -0.368 | <0.001 |

**TABLE 3** Factors associated with Short-Form 36-item questionnaire (SF-36) among patients in the multivariate analysis.
### Risk Factors for Low Health-Related Quality of Life

We stratified patients into two groups according to the PCS and MCS with a cut off point of 50 and then explored the relationship between the PCS, MCS, and potential risk factors (Tables 4 and 5). Logistic regression analysis demonstrated that age (OR 1.032, 95% CI 1.000-1.064), length from discharge to follow-up (OR 0.971, 95% CI 0.951-0.991), and AD8 scores (OR 1.203, 95% CI 1.039-1.398) were significant factors associated with a poor PCS score. AD8 scores (OR 1.543, 95% CI 1.188-2.004) were a significant determinants associated with an MCS<50 in COVID-19 patients.

**TABLE 4** Logistic regression analysis of COVID-19 patients with a physical component summary (PCS)<50.
### TABLE 5 | Logistic regression analysis of COVID-19 patients with a mental component summary (MCS)<50.

|                          | OR   | 95% CI       | P-value |
|--------------------------|------|--------------|---------|
|                          | Lower|             | Upper              |
| Age                      | 1.032| 1.000        | 1.064   | .047 |
| Gender Female            | 1.435| .711         | 2.894   | .313 |
| Clinical subtype         |      |              |         |     |
| Mild                     |      |              |         | .109 |
| Moderate                 | .411 | .099         | 1.709   | .222 |
| Severe or critical       | .842 | .180         | 3.935   | .827 |
| Length from discharge to follow-up | .971 | .951 | .991 | .005 |
| Coronary heart diseases  | 7.293| .765         | 69.514  | .084 |
| AD8 scores               | 1.205| 1.039        | 1.398   | .014 |

**Discussion**

Previous evidence suggests that COVID-19 is a multi-system disease that causes impaired lung and physical function, reduced quality of life, and emotional distress[17]. A recent study revealed the sequelae of COVID-19 patients at 6-month after infection, including fatigue or muscle weakness, sleep difficulties, and anxiety or depression[18]. However, it is unclear whether the society and life of COVID-19 survivors can be restored to a healthy state. Our study examines the HRQoL of COVID-19 survivors at six months of follow-up and reveals its influencing factors and determinants, which provide potential guidance for improving the quality of life of COVID-19 discharged patients.

Comparing the results of this study with the Chinese norm, after six months in COVID-19 rehabilitation patients, the scores of the eight dimensions were significantly lower. This is different from the study by Chen KY [9], who found that the scores of BPGH, VT, and MH were higher than the norm subjects after one month. Recently, studies have reported some sequelae in Covid-19 survivors, including headache, chest pain, and joint pain, among others. Ahmed H[19] found that lung function abnormalities, psychological impairment and reduced exercise capacity were common in SARS and MERS survivors. In this study, we also found that physical functioning, limitation due to physical problems, and general health remained poor in COVID-19 survivors. In addition, studies[20] [5] have reported that fatigue is the common symptom in COVID-19 survivors, which is consistent with our study. We found some decrease in the vitality of the patients.
In a study on SARS[21], people avoided contact with patients who had recovered because of fear of infection. Coincidentally, Dong Liu[22] found that there was fear, stigmatization and discrimination against discharged patients with COVID-19 survivors in Wuhan. COVID-19 patients had poor psychiatric condition after one month of rehabilitation, and most of the patients had post-traumatic stress disorder, anxiety, depression, sleep disorders, and loneliness[23]. Our study found that even after six months of rehabilitation, the social function, role limitation due to emotional problems, and mental health of patients were still lower than those of the general population, which shows that the mental rehabilitation of patients is a long process that requires the attention of family, society, and the scientific community. Data reported in the scientific literature has demonstrated that coronaviruses have neuroinvasive capacities since they can spread from the respiratory tract to the central nervous system[24]. Blood-brain barrier deterioration in older adults leaves them more susceptible to neuroinvasion during SARS-CoV-2 infection[25]. In addition, study[26] found revealed possible disruption to micro-structural and functional brain integrity in the recovery stages of COVID-19, suggesting the long-term consequences of SARS-CoV-2. In the 6-month follow-up study, we found the AD8 is an independent predictor of MCS and PCS in this study, which may explain that the cognitive impairment and dementia was the independent predictor of COVID-19 survivors.

Abnormalities in DLCO indicated pulmonary fibrosis or a late phase in the course of recovery[27]. According to a previous report, 9 patients (16.36%) had impaired DLCO at 3 months after recovered from COVID-19[28]. At 6-months after discharge, 110 patients (32.35%) were found to have DLCO impairment, and were negatively correlated with PF, RP, GH, and SF. This shows that long-term lung function impairment will reduce the quality of life. An early rehabilitation programme following AECOPD led to improvement in quality of life up to 6 months[29]. Pulmonary rehabilitation has also been shown to increase exercise capacity, muscle strength, and health-related quality of life in several populations with respiratory conditions[30]. Respiratory rehabilitation can improve respiratory function, QoL and anxiety of elderly patients with COVID-19[31].

Oestrogens and progesterone exert a profound and broad effect on brain neurochemistry and brain function and interact with early life stress and genetic risk for depression among woman[32]. In addition, a masculine gender identity, which includes personality traits of assertiveness, independence, and self-sufficiency, was positively associated with improvements in participants’ mental health[33]. Due to gender differences, female survivors may experience a long time in the recovery of mental health, and we should pay more attention to female psychological recovery in future studies.

We acknowledge some of the limitations of our study. First, we were unable to compare the data we recruited for COVID-19 survivors in Wuhan with the general population in Wuhan during the same period, for objective reasons. Second, our study did not involve children. Finally, the design of our study is cross-sectional and should be followed up over time in future studies.

**Conclusion**

Our study revealed the influencing factors and determinants of HRQoL for COVID-19 survivors at the sixth month of follow-up, including age, sex, length from discharge to follow-up, AD8 score, and DLCO. AD8 scores was common predictors of PCS and MCS, and predicted poorer physical and psychological quality of life. Chinese patients with COVID-19 have significant HRQoL impairment, and we recommend long-term monitoring in future studies.

**Declarations**

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**Authors' contributions**

ZDZ, JWG, JHZ, and QYD were the main supervisor and initiator of this study and involved in study conception and design. LJZ, BF, QW and YTL were involved in study execution and acquisition of data. JJH, QLL, XHZ, XZ and XTX contributed to data analysis and interpretation. MXL and LQH drafted the manuscript. DWZ, ZHH, HW revised the manuscript. All authors provided substantial intellectual contributions and approved the final version of the manuscript.
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Availability of data and materials

After publication, the data will be made available to others on reasonable requests to the corresponding author. A proposal with detailed description of study objectives and statistical analysis plan will be needed for evaluation of the reasonability of requests. Additional materials might also be required during the process of evaluation. Deidentified participant data will be provided after approval from the corresponding author.

Ethics approval and consent to participate

This study was approved by the ethical committees of Guangdong provincial hospital of traditional Chinese medicine, Guangzhou, China (GPHCM; No. BF2020-205-01). All participants had signed informed consent forms.

Consent for publication

Not applicable.

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Abbreviations

BMI: Body mass index; HRQOL: Health-related quality of Life; MCS: Mental component summary; PCS: Physical component summary; PF: physical functioning; RP: role-physical limitation; BP: bodily pain; general health; VT: vitality; SF: social functioning; RE: role-emotional limitation; MH: mental health;

References

1. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, Ippolito G, McHugh TD, Memish ZA, Dromsten C, et al: The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China. International Journal of Infectious Diseases 2020, 91:264-266.
2. WHO Coronavirus Disease (COVID-19) Dashboard [https://covid19.who.int/table]
3. Brandão Neto D, Fornazieri MA, Dib C, Di Francesco RC, Doty RL, Voegels RL, Pinna FR: Chemosensory Dysfunction in COVID-19: Prevalences, Recovery Rates, and Clinical Associations on a Large Brazilian Sample. Otolaryngol Head Neck Surg 2020:194599820954825.
4. Otte MS, Eckel HNC, Poluschkin L, Klussmann JP, Luers JC: Olfactory dysfunction in patients after recovering from COVID-19. Acta Otolaryngol 2020:1-4.
5. Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, Dong W: Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect* 2020.

6. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009, 6:e1000097.

7. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, Baker P, Smith E, Buchbinder R: Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012, 65:934-939.

8. Carfì A, Bernabei R, Landi F, for the Gemelli Against C-P-ACSG: Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020, 324:603-605.

9. Chen KY, Li T, Gong FH, Zhang JS, Li XK: Predictors of Health-Related Quality of Life and Influencing Factors for COVID-19 Patients, a Follow-Up at One Month. *Front Psychiatry* 2020, 11:668.

10. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). *Chin Med J (Engl)* 2020, 133:1087-1095.

11. Li L, Wang H, Shen Y: Development and psychometric tests of a Chinese version of the SF-36 Health Survey Scales. *Zhonghua Yu Fang Yi Xue Za Zhi* 2002, 36:109-113.

12. Ware J, Ma K, Keller SD: SF-36 Physical and Mental Health Summary Scales: a User's Manual. 1993, 8:23-28.

13. Usarel C, Dokuzlar O, Aydin AE, Soysal P, Isik AT: The AD8 (Dementia Screening Interview) is a valid and reliable screening scale not only for dementia but also for mild cognitive impairment in the Turkish geriatric outpatients. *Int Psychogeriatr* 2019, 31:223-229.

14. Aji BM, Lamer AJ: Cognitive assessment in an epilepsy clinic using the AD8 questionnaire. *Epilepsy Behav* 2018, 85:234-236.

15. Horváth I, Barnes PJ, Loukides S, Sterk PJ, Högman M, Olin AC, Amann A, Antus B, Baraldi E, Bikov A, et al: A European Respiratory Society technical standard: exhaled biomarkers in lung disease. *Eur Respir J* 2017, 49.

16. Rui W, Cheng W, Ma XQ, Zhao YF, Yan XY, Jia H: Health-related quality of life in Chinese people: a population-based survey of five cities in China. *Scand J Public Health* 2011, 39:410-418.

17. Barker-Davies RM, O’Sullivan O, Senaratne KPP, Baker P, Cranley M, Dharm-Datta S, Ellis H, Goodall D, Gough M, Lewis S, et al: The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *British Journal of Sports Medicine* 2020, 54:949-959.

18. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, Kang L, Guo L, Liu M, Zhou X, et al: 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021, 397:220-232.

19. Ahmed H, Patel K, Greenwood DC, Halpin S, Lewthwaite P, Salawu A, Eyer L, Breen A, O’Connor R, Jones A, Sivan M: Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. *J Rehabil Med* 2020, 52:jrm00063.

20. Halpin SJ, McIvor C, Whyatt G, Adams G, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, et al: Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol* 2020.

21. Person B, Sy F, Holton K, Govert B, Liang A: Fear and stigma: the epidemic within the SARS outbreak. *Emerg Infect Dis* 2004, 10:358-363.

22. Liu D, Baumeister RF, Veilleux JC, Chen C, Liu W, Yue Y, Zhang S: Risk factors associated with mental illness in hospital discharged patients infected with COVID-19 in Wuhan, China. *Psychiatry Res* 2020, 292:113297.

23. González-Sanguino C, Ausín B, Castellanos MÁ, Saiz J, López-Gómez A, Ugidos C, Muñoz M: Mental health consequences during the initial stage of the 2020 Coronavirus pandemic (COVID-19) in Spain. *Brain, Behavior, and Immunity* 2020, 87:172-176.

24. Desforges M, Le Coupanec A, Stodola JK, Meessen-Pinard M, Talbot PJ: Human coronaviruses: viral and cellular factors involved in neuroinvasiveness and neuropathogenesis. *Virus Res* 2014, 194:145-158.
25. Hascup ER, Hascup KN: Does SARS-CoV-2 infection cause chronic neurological complications? *Geroscience* 2020, 42:1083-1087.

26. Lu Y, Li X, Geng D, Mei N, Wu PY, Huang CC, Jia T, Zhao Y, Wang D, Xiao A, Yin B: Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study. *EClinicalMedicine* 2020, 25:100484.

27. Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G, Ko FW, Chan MC, Chan DP, Tong MW, et al: Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax* 2005, 60:401-409.

28. Zhao YM, Shang YM, Song WB, Li QQ, Xie H, Xu QF, Jia JL, Li LM, Mao HL, Zhou XM, et al: Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* 2020, 25:100463.

29. Ko FW, Dai DL, Ngai J, Tung A, Ng S, Lai K, Fong R, Lau H, Tam W, Hui DS: Effect of early pulmonary rehabilitation on health care utilization and health status in patients hospitalized with acute exacerbations of COPD. *Respirology* 2011, 16:617-624.

30. Grigoletto I, Cavalheri V, Lima FF, Ramos EMC: Recovery after COVID-19: The potential role of pulmonary rehabilitation. *Braz J Phys Ther* 2020.

31. Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y: Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study. *Complement Ther Clin Pract* 2020, 39:101166.

32. Mauvais-Jarvis F, Bairey Merz N, Barnes PJ, Brinton RD, Carrero JJ, DeMeo DL, De Vries GJ, Epperson CN, Govindan R, Klein SL, et al: Sex and gender: modifiers of health, disease, and medicine. *Lancet* 2020, 396:565-582.

33. Duggleby W, Williams A, Ghosh S, Moquin H, Ploeg J, Markle-Reid M, Peacock S: Factors influencing changes in health related quality of life of caregivers of persons with multiple chronic conditions. *Health Qual Life Outcomes* 2016, 14:81.

**Figures**

**COVID-19 survivors vs Chinese population norms**

![Graph](image)

**Figure 1**

Mean scores in SF-36 for COVID-19 patients vs Chinese population norms. PF, physical functioning; SF, social functioning; RP, role limitation due to physical problems; RE, role limitation due to emotional problem; MH, mental health; BP, bodily pain; VT, vitality, GH, general health. *P<0.05