Influence of transitional care on the clinical manifestations among patients with COVID-19: A single-center, double-blinded, randomized survey

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Abstract. Pneumonia and acute respiratory distress syndrome are the major complications of coronavirus disease 2019 (COVID-19). Transitional care is indispensable in successfully transitioning patients with COVID-19 from hospital to home and preventing adverse events of this disease. The purpose of the present study was to analyze the effects of transitional care on improvements in inflammation and pulmonary function in patients with COVID-19. Data of all hospitalized patients with COVID-19 (n=242) discharged from Mudanjiang Medical University (Mudanjiang, China) between May 2020 and October 2020 were retrospectively collected. Patients with COVID-19 had been hospitalized and assigned to receive transitional care (n=126) or usual care (n=116) and were followed up for 12 months. Hospital stay, inflammation and pulmonary function were compared in patients with COVID-19 between the transitional care and usual care group. Transitional care significantly improved physical symptoms, anxiety, depression and empathy of the patients for other patients affected. Compared to the usual care group, marked improvements in typical symptoms, including dyspnea, asthenia, cough, nausea, chest pain, myalgia, headache, fever, diarrhea, chest pain, dizziness, conjunctivitis, as well as disorders of smell and taste, were observed in the transitional care group. Patients in the transitional care group had a shorter hospital stay than those patients in the usual care group. Furthermore, transitional care decreased inflammation and ameliorated pulmonary function in patients with COVID-19. In conclusion, transitional care has an essential role in the improvement of physical symptoms, inflammation and pulmonary function in patients with COVID-19 [Chinese Clinical Trial Registry (ChiCTR) registration no. ChiCTR2200060295; 26.05.2022].

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Introduction

Coronavirus disease 2019 (COVID-19) has spread rapidly across the globe, with high rates of transmission and substantial sequelae (1). Patients infected with COVID-19 display various symptoms ranging from mild, self-limited respiratory disease to moderate to severe progressive pneumonia (2). The main clinical symptoms of patients with COVID-19 include fever, cough, myalgia, fatigue, expectoration, dyspnea, headache, diarrhea, nausea and vomiting (3). Of note, most patients with COVID-19 present without fever and numerous patients do not have any abnormal radiologic findings (4,5). At present, although vaccines to prevent COVID-19 have been developed with unprecedented speed (6), the increase of infected patients with existing illnesses and multi-morbidity cause massive loss of life and economic hardship (7). Worldwide, the cumulative number of COVID-19 cases has reached 5,139,555,910 and the number of COVID-19-related deaths is now thought to exceed 15 million as of May 7, 2022. In China, 865,592 COVID-19 cases have been recorded and the number of deaths is only 15,417, as of May 7, 2022.

A wide range of clinical outcomes has been observed in patients with COVID-19 after various treatment strategies (8). Nursing care of patients with COVID-19 is necessary, supportive and beneficial, which includes a strong focus on mitigating the spread of infection to others and the community (9). Transitional care is an important aspect of the healthcare systems, and yet, it is necessary to improve the quality of life of patients (10). Transitional care has an essential role in the response to COVID-19 by responding rapidly and flexibly. Transitional care ensures protocols for symptom management to provide psychosocial care and communication with patients (11). Of note, transitional care is indispensable to successfully guide patients at discharge or post-discharge to prevent adverse events in patients with COVID-19, making it essential for efficient medical and nursing practice (12).

The most common symptoms and complications of patients with COVID-19 are inflammation and respiratory infection (13). Inflammation and the innate immune system have

been recently recognized as pivotal players in the progression of COVID-19, characterized by significantly elevated levels of pro-inflammatory cytokines (14). In the present study, the effects of transitional care on psychological symptoms, inflammation, and pulmonary function in patients with COVID-19 were investigated. The quality of life, recurrence rate, duration of hospital stay and psychological symptoms such as depression, anxiety, fear, perception of helplessness and worry were also compared in COVID-19 patients between transitional care and usual care group.

Patients and methods

Patient and public involvement. Patient and public involvement have been central to the design of the present study. All patients with COVID-19 were recruited at the Affiliated Hongqi Hospital of Mudanjiang Medical University (Mudanjiang, China), randomly assigned to receive transitional care or usual care and followed up for 12 months. All patients were recently diagnosed with mild or moderate COVID-19. All outcomes from each participant were assessed and recorded by medical staff. The results of the present study were disseminated to the study researchers in written form, which comprised professionals within the area of COVID-19.

Case definition. The severity of COVID-19 was categorized into four types according to officially published guidelines in China (15): a) Mild type: Asymptomatic or certain upper respiratory tract infection signs and no evidence of pneumonia on imaging; b) Moderate type: Febrile respiratory symptoms and imaging findings of pneumonia; c) Severe type: Disease progression with danger signs (respiratory rate of >30 beats/min, oxygen saturation of <93%, oxygen partial pressure of >300 mmHg, or lung imaging indicating significant progression of >50% within 24-48 h); d), Critical type: Shock or organ failure requiring intensive care.

Study design. The present clinical trial was a randomized, double-blinded, single-center study. A total of 252 patients with recently diagnosed mild or moderate COVID-19 were recruited at the Affiliated Hongqi Hospital of Mudanjiang Medical University (Mudanjiang, China) between May 2020 and October 2020. A total of 10 patients were excluded according to selection criteria. Patients were randomly assigned to transitional care (n=126) or usual care (n=116) and followed up for 12 months. Included were patients with COVID-19 who met the following criteria: i) Aged 18 years or above; ii) diagnosis of mild to moderate COVID-19 infection; iii) hospitalization duration of less than two days; iv) patients without any physical disability or depressive disease. Exclusion criteria were patients in intensive care unit admission, advanced age with multiple comorbidities, patients with severe COVID-19, individuals with dementia or delirium and patients with advanced or metastatic tumors. The protocol was reviewed and approved by the ethics committees of Mudanjiang Medical University (Mudanjiang, China). All patients provided written informed consent. The trial was entered in the Chinese Clinical Trial Registry (ChiCTR); registration no. ChiCTR2200060295; 26.05.2022.

Transitional care. The transitional care program is designed based on the Omaha System (16), which is a method to describe the needs of patients and to solve patient problems. In brief, the Omaha System includes a problem classification scheme, intervention scheme and problem rating scale. The transitional care intervention scheme also includes guidance, teaching and counseling, clinical treatments, postoperative management and four broad surveillance categories. Transitional care of predischarge interventions includes early assessment after hospital admission, medication reconciliation and planning of patient education in sporting and dieting upon discharge.

Biochemical analysis. Blood samples were collected from each patient with COVID-19. Routine blood tests and arterial blood gas tests were performed for all patients and the following parameters were evaluated: D-dimer, lymphocyte count, alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin, platelets, white blood cells, lactate, creatinine, hemoglobin, and saturation of peripheral oxygen/fraction of inspired oxygen ratio.

Inflammatory cytokine assay. Serum levels of C-reactive protein (CRP), interleukin-1β (IL-1β) (cat. no. KAC1211), IL-6 (cat. no. KHC0061), IL-8 (cat. no. BMS204-3), IL-17 (cat. no. A35611) and TNF-α (cat. no. BMS223-4) were measured using ELISA kits (Thermo Fisher Scientific, Inc.) according to the manufacturer's protocol.

Mental health symptoms. The severity of symptoms of depression in each patient with COVID-19 was assessed using the Patient Health Questionnaire (PHQ-9) (17). The total score of PHQ-9 ranges from 0 to 27 (depressive symptoms, score ≥5; moderate to severe depression, score ≥10). Anxiety in patients with COVID-19 was evaluated using the Generalized Anxiety Disorder (GAD-7) questionnaire (18). The total score of GAD-7 ranges from 0 to 21 (anxiety symptoms, score ≥5; moderate to severe anxiety, score >8) (19). Stress, fear, perception of helplessness, worry and empathy of patients with COVID-19 were evaluated using standard questionnaires (PSS 10, and DASS 21) as described previously (20).

Quality of life. Quality of life of patients with COVID-19 was assessed using the SF-36 questionnaire (21). The SF-36 questionnaire includes 36 multiple-choice questions by measuring 8 distinct domains (physical functioning, physical health, general health perceptions, emotional problems, energy/fatigue, emotional well-being, social functioning and bodily pain). Scores of quality of life range from 0 to 100 with a higher score indicating a higher quality of life.

Pulmonary function tests. Airway function, including spirometry, pulmonary volume and diffusing capacity, was measured in all patients using a flow spirometer (MasterScreen; Jaeger) according to the manufacturer's protocol. Parameters of pulmonary function, including total pulmonary capacity (TLC), forced vital capacity (FVC), residual volume, forced expiratory volume in 1 sec (FEV_1), FEV_1/FVC and diffusing capacity of the pulmonary for carbon monoxide (D_{LCO}) were measured according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines (22).

Table I. Patient demographics and baseline clinical characteristics.

Characteristic	Usual care (n=116)	Transitional care (n=126)	P-value
Age, years	52.5±10.5	52.0±11.5	0.91
Sex			
Male	62 (25.6)	66 (27.3)	0.96
Female	58 (24.0)	56 (23.1)	0.85
BMI, kg/m^2	28.0±4.2	28.2±4.5	0.96
COVID-19 severity			
Moderate	46 (36.5)	51 (40.1)	0.87
Mild	70 (63.5)	75 (59.9)	0.92
Clinical parameters			
Respiratory rate, cycles/min	37.4±3.6	37.2±3.2	0.98
Heart rate, beats/min	97.5±14.6	96.5±13.5	0.95
Systolic blood pressure, mmHg	128.5±14.8	126.8±16.5	0.93
Hospital admission symptoms			
Cough	86 (74.1)	88 (69.8)	0.85
Fever >38°C	72 (62.1)	76 (60.3)	0.96
Shortness of breath	56 (48.3)	62 (49.2)	0.91
Myalgia	40 (34.5)	45 (35.7)	0.92
Laboratory parameters (normal ranges)			
Hemoglobin, g/dl (12-17)	12.8±0.5	12.4±0.7	0.90
Creatinine, mg/dl (0.6-1.2)	1.1±0.3	1.2±0.4	0.93
Lactate, mmol/l (1.0-2.5)	1.8±0.6	1.7±0.5	0.98
INR (0.8-1.2)	1.4±0.3	1.5±0.4	0.96
White blood cells, cells/mm^3 (4-10)	22.4±4.8	23.8±5.7	0.90
Lymphocytes, 10^9/l (1.1-3.2)	0.9±0.3	1.0±0.4	0.99
Platelets, cells/mm^3 (150-450)	214.5±54.2	225.8±60.4	0.86
d-dimer, mcg/ml (<1)	2.8±1.2	3.0±1.4	0.95
ALT, μ/l (9-50)	29.5±8.8	31.2±9.4	0.97
AST, μ/l (15-40)	29.2±12.6	28.5±13.0	0.93
Total bilirubin, μmol/l (0-26)	15.5±6.0	16.4±6.6	0.90
Albumin, μ/l (15-40)	26.8±6.8	28.4±7.3	0.99
Positive-end-expiratory-pressure, cm x H_2O	11.8±3.6	12.4±4.2	0.94
SpO_2/FiO_2 ratio	155.4±30.8	162.6±33.5	0.95

Values are expressed as the mean ± standard deviation or n (%). BMI, body mass index; INR, international normalization ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SpO_2/FiO_2, saturation of peripheral oxygen/fraction of inspired oxygen; COVID-19, coronavirus disease 2019.

Pulmonary function was analyzed using SentrySuite software V03.0.5 (Vyaire Medical). The 6-min walking test (6MWT) was evaluated according to ATS/ERS guidelines (23).

Symptom score. The symptom score of the patients with COVID-19 was evaluated from their electronic medical records (24). The severity of symptoms was scored from 0 to 10 points. The 10-scale symptom scoring system for patients with COVID-19 included nausea, dyspnea, chest pain, cough, asthenia, myalgia, dizziness, conjunctivitis, loss of appetite and diarrhea. Lower scores indicated a lower level of symptoms.

Statistical analyses. Values are expressed as the mean ± standard deviation or n (%). The data were analyzed using Stata V.13.0 (StataCorp LP). Data were analyzed using SPSS v20 software (IBM Corporation). Differences between two groups were analyzed by using the χ^2 or Fisher's exact test for categorical variables, the two-samples t-test or Wilcoxon rank-sum test for continuous variables as applicable. P<0.05 was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 252 patients with COVID-19 pneumonia were included in the analysis. A total of 10 patients were excluded according to the exclusion criteria. Demographic and baseline clinical characteristics of the patients with COVID-19 (n=242) are presented in Table I. The most common symptoms of

Table II. Baseline levels of inflammatory cytokines in patients with coronavirus disease 2019 (mg/l).

Parameter	Usual care	Transitional care	P-value
CRP	93.6±8.7	94.8±10.2	0.84
IL-1β	78.2±12.0	75.7±12.1	0.94
IL-6	78.2±12.0	80.3±14.4	0.95
IL-8	68.5±16.4	71.2±18.8	0.96
IL-17	124.5±25.8	132.0±22.5	0.83
TNF-α	22.4±5.7	23.0±4.9	0.88

Values are expressed as the mean ± standard deviation. CRP, C-reactive protein; IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α.

Table III. Baseline pulmonary function in patients with coronavirus disease 2019.

Pulmonary function parameter	Usual care	Transitional care	P-value
FEV1/FVC, %	86.0±13.6	84.3±11.9	0.90
TLC, l	4.5±1.5	4.4±1.3	0.88
TLC, % pred	105.2±16.7	102.2±12.8	0.93
FVC, l	2.7±0.5	2.7±0.6	0.97
FVC, % pred	93.2±18.7	91.8±15.4	0.95
FEV_1, l	2.80±0.63	2.72±0.57	0.88
FEV1, l pred	95.6±17.2	92.6±14.8	0.86
DLCO, % pred	94.1±15.8	93.5±16.2	0.98
P_{Imax}, kPa	8.4±1.9	8.2±1.7	0.97
P_{Emax}, kPa	10.0±3.0	10.2±3.2	0.98

Values are expressed as the mean ± standard deviation. FEV1, forced expiratory volume in 1 sec; pred, predicted; FVC, forced vital capacity; TLC, total lung capacity; DLCO, diffusing capacity of the lung for carbon monoxide; P_{Imax}, maximal inspiratory pressure; P_{Emax}, maximal expiratory pressure.

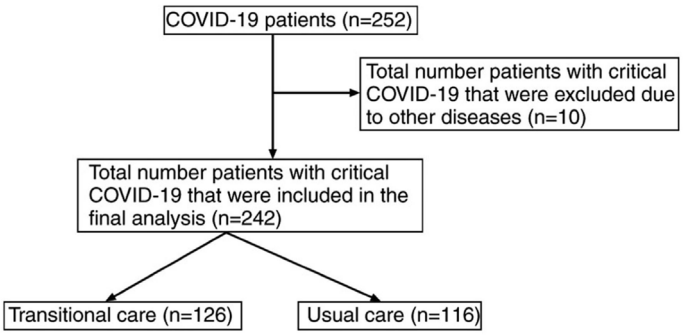

Figure 1. Study flowchart of patients with COVID-19. COVID-19, coronavirus disease 2019.

the patients were fever, dyspnea, asthenia and cough. The cohort included 128 male (52.9%) and 114 female patients (47.1%) with a median age of 56.0 years (range, 45.0-65.0 years). The patients with COVID-19 were assigned to receive either transitional care (n=126) or usual care (n=116) (Fig. 1). All patients were generally well balanced at the time of enrollment, i.e. there were no significant differences between the two groups.

Inflammation in patients with COVID-19. Inflammatory cytokines, including CRP, IL-1β, IL-6, IL-8, IL-17 and TNF-α, analyzed in patients with COVID-19 at discharge, were compared between the two groups. The baseline levels of the inflammatory cytokines in the two groups are listed in Table II. As indicated in Fig. 2A, a decrease of CRP in patients with COVID-19 in the transitional care group compared with that in the usual care group was present on day 7, 14 and 21 during hospitalization. A lower serum level of IL-1β was observed in patients with COVID-19 in the transitional care group as compared with that in the usual care group on day 7, 14 and 21 during hospitalization (Fig. 2B). The outcomes demonstrated

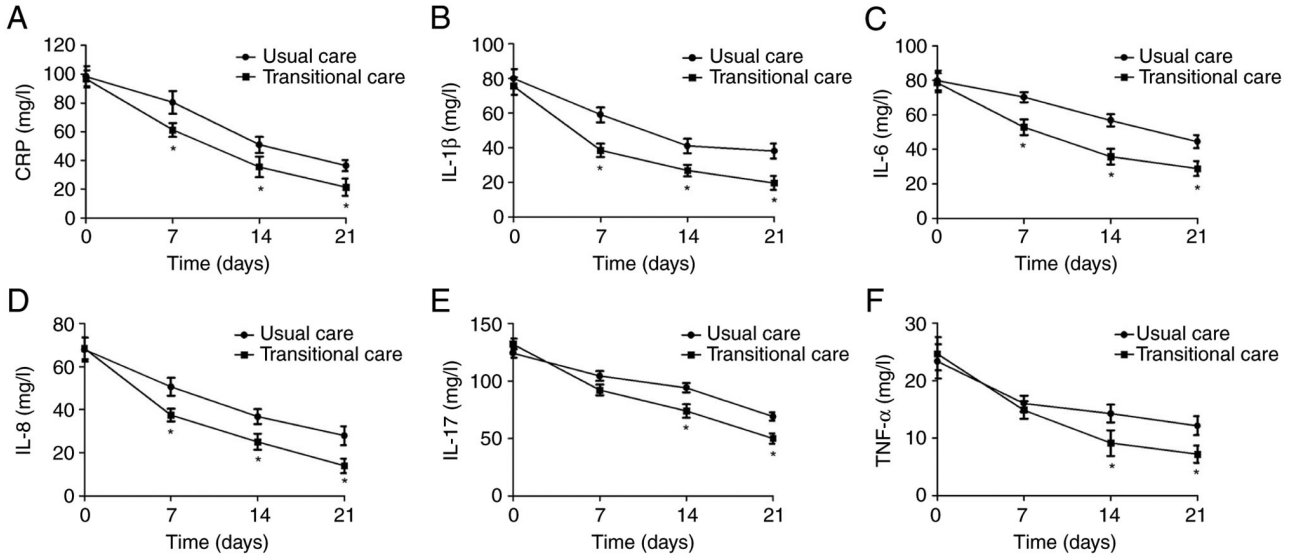

Figure 2. Markers of inflammation in patients admitted to the hospital for COVID-19. (A-F) COVID-19-infected patients have increased plasma proinflammatory cytokines, including (A) CRP, (B) IL-1β, (C) IL-6, (D) IL-8, (E) IL-17 and (F) TNF-α as indicated by ELISA. *P<0.05 vs. usual care. CRP, C-reactive protein; IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α; COVID-19, coronavirus disease 2019.

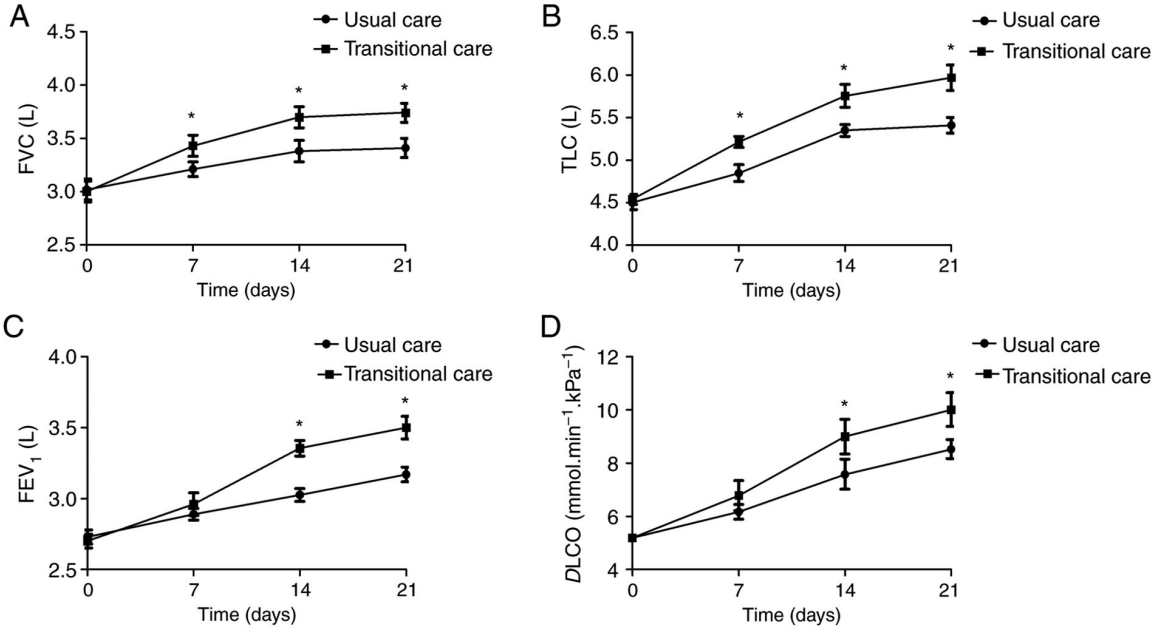

Figure 3. Pulmonary function test in patients with COVID-19 compared between usual care and transitional care groups. (A) FVC, (B) TLC, (C) FEV1 and (D) D_{LCO} were relatively high in patients with COVID-19. *P<0.05 vs. usual care. FVC, forced vital capacity; TLC, total pulmonary capacity; FEV1, forced expiratory volume in 1 sec; D_{LCO}, diffusion capacity for carbon monoxide; COVID-19, coronavirus disease 2019.

that IL-6 and IL-8 levels were markedly decreased in patients with COVID-19 on days 7, 14 and 21 of hospitalization (Fig. 2C and D). Compared with the usual care group, transitional care decreased the serum levels of IL-17 and TNF-α in patients with COVID-19 on days 14 and 21 of hospitalization (Fig. 2D-F). At discharge (median, 21.5; range, 14.5-27.5 days after the day of hospitalization), no significant differences were observed between the two groups (data not shown).

Pulmonary function in patients with COVID-19. Pulmonary function was recorded in patients with COVID-19 between the transitional care and usual care group. The baseline parameters of pulmonary function in the two groups are listed in Table III. Fig. 3 provides the results of pulmonary function in patients with COVID-19 in the two groups over the course of hospitalization. Patients in transitional care had better pulmonary function than those in the usual care group. The mean values of FVC, TLC, FEV1 and D_{LCO} were relatively higher in patients with COVID-19 in the transitional care group compared to those in the usual care group. Only a small number of the patients required oxygen supplementation in the two groups and none of the patients was intubated or admitted to the intensive care unit. Pulmonary function of patients post-discharge did not significantly differ between the two groups (P>0.05; data not shown).

Table IV. Mental and physical state of patients with coronavirus disease 2019.

A, At discharge

Item	Usual care	Transitional care	P-value
Quality of life[a]	74.0±8.2	82.8±12.4	0.032
Hospital stay, days	15.5±4.5	12.0±3.5	0.046
Fear	46 (39.7)	32 (25.4)	0.017
Feeling/perception of helplessness	58 (50.0)	25 (19.8)	0.0028
Worry	72 (62.1)	30 (23.8)	0.0030
Empathy of the patients for other patients affected	50 (43.1)	21 (16.7)	0.040
6MWD, m	465±56	582±64	0.010

B, Post-discharge

Item	Usual care	Transitional care	P-value
Quality of life[a]	83.3±7.6	89.5±8.5	0.048
Fear	15 (12.9)	5 (4.0)	0.013
Feeling/perception of helplessness	18 (15.5)	10 (7.9)	0.024
Worry	14 (12.1)	7 (5.6)	0.016
Empathy of the patients for other patients affected	10 (8.6)	6 (4.8)	0.038
6MWD, m	618±94	676±104	0.042

C, At discharge

Item	Usual care	Transitional care	P-value
Anxiety (GAD-7)	15.8±6.9	10.2±4.0	0.032
Depression (PHQ-9)	16.2±5.2	9.2±4.5	0.027

D, Post-discharge (during three months)

Item	Usual care	Transitional care	P-value
Anxiety (GAD-7)	8.4±3.1	5.0±2.5	0.020
Depression (PHQ-9)	7.9±2.8	4.7±1.5	0.045

Values are expressed as the mean ± standard deviation or n (%). [a]Assessed with the SF-36 questionnaire (score range, 0-100). 6MWD, 6-min walking distance; PHQ-9, Patient Health Questionnaire 9; GAD-7, Generalized Anxiety Disorder 7 questionnaire.

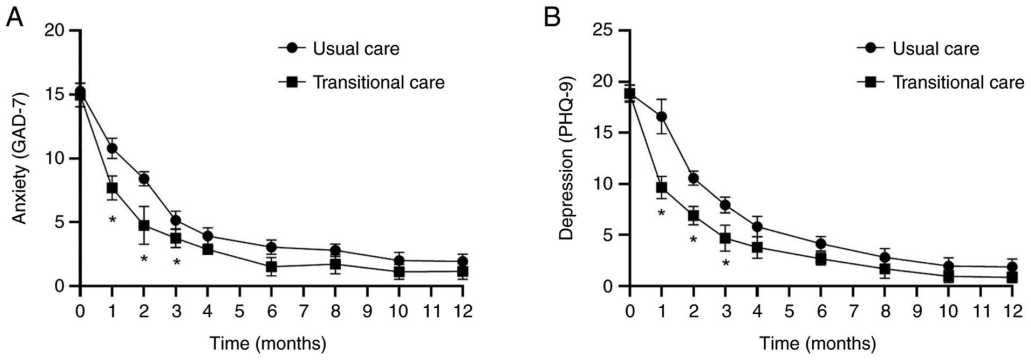

Figure 4. Mean score of changes of mental health status in patients with COVID-19 compared between the usual care and transitional care group. (A) The score of depression in patients with COVID-19 was assessed using PHQ-9 in the 12-month follow-up. (B) Score of anxiety in patients with COVID-19 was assessed using GAD-7 questionnaire in 12-month follow-up. *P<0.05 vs. usual care. PHQ-9, patient health questionnaire; GAD-7, generalized anxiety disorder; COVID-19, coronavirus disease 2019.

Table V. Symptoms/complaints of patients with coronavirus disease 2019 at discharge.

Adverse event	Usual care	Transitional care	P-value
Dyspnea	18 (15.5)	9 (7.1)	0.037
Asthenia	16 (13.8)	9 (7.1)	0.043
Cough	26 (22.4)	16 (12.7)	0.035
Headache	10 (8.6)	5 (4.0)	0.016
Chest pain	32 (27.6)	20 (15.9)	0.019
Nausea	17 (14.7)	10 (7.9)	0.048
Fever	86 (74.1)	60 (47.6)	0.011
Myalgia	45 (38.8)	32 (25.4)	0.045
Diarrhea	15 (12.9)	8 (6.3)	0.034
Dizziness	20 (17.2)	13 (10.3)	0.030
Conjunctivitis	23 (19.8)	13 (10.3)	0.040
Loss of smell	36 (31.0)	25 (19.8)	0.025
Loss of taste	38 (32.8)	27 (21.4)	0.046

Values are expressed as n (%).

Table VI. Recurrence of patients with coronavirus disease 2019 post-discharge.

Parameter	Usual care	Transitional care	P-value
Recurrence	10 (8.6)	3 (2.4)	0.011
Oxygen therapy (at the hospital)	1 (0.7)	4 (3.4)	0.044

Values are expressed as n (%).

Mental and physical state of patients with COVID-19. Patients with COVID-19 had reduced levels of physical function and fitness in comparison to healthy controls. Physical symptoms, including the quality of life and hospital stay, as well as stress, fear, perception of helplessness, worry and empathy of the patients for other patients affected were recorded for patients with COVID-19 and compared between the transitional care and usual care groups. Transitional care significantly improved the quality of life and decreased stress, fear, helplessness, worry and empathy in patients with COVID-19 at discharge or post-discharge compared to usual care (Table IV). Transitional care also decreased stress, fear, helplessness, worry and empathy of the patients for other human patients affected in patients with COVID-19 post-discharge compared with that in the usual care group (Table IV). As indicated in Table V, patients with COVID-19 at discharge in the transitional care group exhibited significantly decreased levels of depression and anxiety in comparison with those in the usual care group at the indicated time-point (P<0.05). Transitional care also improved depression and anxiety in patients with COVID-19 during the first 3 months post-discharge. Data of patients with COVID-19 with transitional care indicated that no significant differences in depression and anxiety were present between the two groups at the 12-month follow-up (Fig. 4). In addition, patients in the transitional care group had a better 6-min walking distance than those in the usual care group.

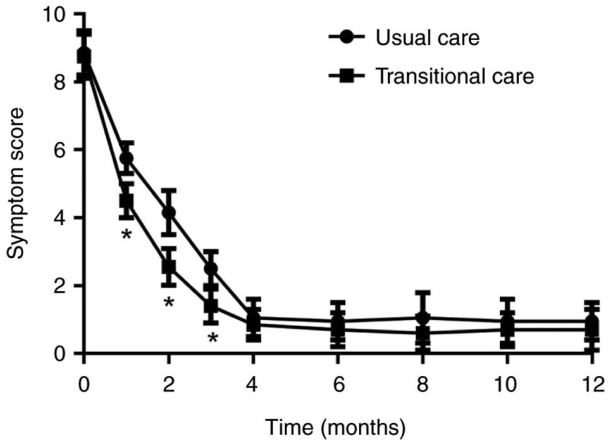

Figure 5. Summary curves of total symptoms scores in patients with COVID-19. Symptoms scores were compared in patients with COVID-19 at discharge between the usual care and transitional care groups. *P<0.05 vs. usual care. COVID-19, coronavirus disease 2019.

Symptoms and complaints in patients with COVID-19 at discharge and post-discharge. Symptoms/complaints in patients with COVID-19 at discharge or post-discharge were compared between the two groups. Transitional care efficiently improved the most common symptoms/complaints of patients, including dyspnea, asthenia, cough, nausea, chest pain, myalgia, headache, fever, diarrhea, chest pain, dizziness, conjunctivitis, disorders of smell and taste compared to patients in usual care (Table V). There were no significant differences in the most common symptoms for patients post-discharge between the two groups. Symptom scores were higher in the transitional care group than those in the usual care group for patients with COVID-19 during the first three months after discharge (P<0.05), while no significant differences were observed for patients with COVID-19 after 3 months post-discharge (P>0.05; Fig. 5).

Recurrence of patients with COVID-19 post-discharge. The recurrence rate (patients having a relapse/re-infection with COVID-19) of patients with COVID-19 was recorded during the 12-month follow-up. Data revealed that transitional care decreased the recurrence of patients with COVID-19 post-discharge compared with that in the usual care group (Table VI). A total of 3 (2.4%) patients had complications that required readmission to the hospital in the transitional care group, while the number of recurrences of patients with COVID-19 post-discharge was 10 (8.6%). Furthermore, one (0.7%) patient with COVID-19 in the transitional care group and 4 (3.4%) patients with COVID-19 in the usual care group required oxygen therapy again during the recurrence.

Discussion

Care for patients with COVID-19 during hospitalization and discharge may be necessary. The interventions necessary to care for patients with COVID-19 are performed by nurses

under the condition of adequate prevention (25). Adequate transitional care possibly results in good post-discharge outcomes in patients with COVID-19 (12). The present study demonstrated that transitional care not only improved the mental health, inflammation and pulmonary function in patients with COVID-19, but also decreased the adverse events and recurrence of COVID-19.

The pulmonary characteristics in patients with COVID-19 are ground-glass opacity admixed with reticulation and linear opacities, along with signs of architectural distortion and bronchial dilatation (26). The results of a previous study indicated that lymphocyte percentages, neutrophils and CRP may be used as markers for COVID-19, helping to prioritize certain individuals (27). Correlations between severity and levels of IL-1 and IL-18 were previously reported to be useful in COVID-19 treatment (28). Serum IL-6 is one promising novel biomarker for evaluating the severity of COVID-19 (29). In hospitalized patients with severe COVID-19, decreasing IL-17 levels may mitigate the inflammatory response and improve oxygenation, but does not affect the requirement for mechanical ventilation and psychological symptoms (30). Serum concentrations of TNF-α and IL-17A are more elevated in patients with COVID-19, which opens a new field of research for COVID-19 (31). The present results suggested that transitional care efficiently improved the serum levels of inflammatory cytokines, including CRP, IL-1β, IL-6, IL-8, IL-17 and TNF-α, of patients with COVID-19 at discharge. Certain evidence demonstrated that inflammation in certain patients with COVID-19 was closely related to the severity of this disease and subsequent sequelae (32). Overall, the present results indicated that transitional care significantly improved pulmonary function of patients with COVID-19 at discharge and post-discharge. In addition, transitional care decreased inflammatory cytokines in patients with COVID-19 at discharge. Of note, transitional care contributed to the decrease of adverse events and recurrence. However, it remains elusive whether transitional care will progress to symptomatic pulmonary function or if transitional care for COVID-19 may influence the treatment outcome at discharge.

COVID-19 may have caused mental health changes in numerous individuals (33). Certain hospitalized patients who have already been affected by the virus may still receive medical treatment. In the present study, patients with COVID-19 receiving transitional care had markedly improved mental health issues, including depression and anxiety symptoms at discharge or post-discharge. Compared to the control, transitional care markedly improved the emotional wellbeing of the patients, including stress, fear, perception of helplessness, worry and empathy, as determined by using standard questionnaires for patients with COVID-19. All questionnaires on emotions for certain variables were available for each patient with COVID-19. Regarding psychological symptoms in the patients with COVID-19, patients who received management with transitional care had an overall improvement of 92.7%, which was higher compared to the control group, and this has been recognized as one of the best indicators of prognosis. Consistent with previous studies (34,35), the present data indicated that the hospital stay was shorter in the transitional care group, although no significant differences of nausea, chest pain, fever, diarrhea, chest pain, dizziness, conjunctivitis, disorders of smell and taste for patients post-discharge were observed between the transitional care and usual care group. Of note, an inflammatory rebound triggered by an inadequate immune response may constitute an alternative explanation for the recurrence of patients with COVID-19 (36). The results of the present study suggested that transitional care reduced the recurrence of patients with COVID-19, which may be due to the decrease of serum levels of inflammatory cytokines. Data from patients suggested that transitional care improved psychosocial stress, depression and anxiety by post-discharge hospital visits, home health supervision, monitoring of medications and discontinuation of isolation, which may contribute to the decrease of adverse events and recurrence in patients with COVID-19. However, these preliminary data are only supportive and suggest the requirement for further study to determine whether patients with COVID-19 with risk factors of recurrence should be prioritized for transitional care.

Of note, the present study had certain limitations. The study involved transitional care from a single center and may not reflect all the effects of transitional care on the recurrence of patients with COVID-19 in different countries. In addition, although data in the present study indicate that transitional care decreases serum levels of inflammatory cytokines, it cannot be excluded that different populations of patients with COVID-19 with different medical treatments may have different tendencies. Furthermore, it is important to mention that long-term follow-up was not investigated in the present study, at best the efficacy of transitional care has been explored.

In conclusion, the fact that patients with COVID-19 may experience re-activation of the virus or re-infection, as well as potential sequelae of this disease, highlights the importance of transitional care for the management and prevention of the pandemic in the world. The results of the present study indicate that transitional care provides benefits in the recovery of COVID-19 virus-induced inflammation, improving physical symptoms and mental health, as well as decreasing adverse events and recurrence. The present study highlighted the value of transitional care for health care systems, which suggests that transitional care should be developed to ensure better pulmonary function, quality of life, physical symptoms, mental health status and lower recurrence in patients with COVID-19.

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Availability of data and materials

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

Authors' contributions

LLS designed the project, wrote the manuscript and performed data analysis. BXL and JL performed experiments.

CYH designed the study and wrote the manuscript. LLS and CYH authors confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval was granted by the ethics committees of Mudanjiang Medical University (Mudanjiang, China; approval no. 20201001X1). All patients provided written informed consent to participate in the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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