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Original Article

Prone position nursing combined with ECMO intervention prevent patients with severe pneumonia from complications and improve cardiopulmonary function

Min Zhang, Xin Li, Yu Bai

2A ICU, Shanghai General Hospital, Shanghai 201620, China

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Abstract: Objective: To study the application value of prone nursing combined with extracorporeal membrane oxygenation (ECMO) in patients with severe pneumonia. Methods: Altogether 96 patients with severe pneumonia from December 2016 to June 2018 were selected as the research participants, and 48 patients were included in the observation group (OG) to receive prone nursing with ECMO, while the other 48 patients were included in the control group (CG) to receive routine nursing with ECMO. Complications, cardiopulmonary function, VAS, SAS, SDS, MMAS-8 scores and nursing satisfaction were compared. Results: After nursing, the incidence of complications in the OG was lower than that in the CG, LVEDD and LVESD in OG were lower than those in CG, while LVEF, FEV1 and FVC were higher than those in CG. The scores of VAS, SAS and SDS in OG were lower than those in CG. The MMAS-8 score in the OG was higher than that in the CG. The total nursing satisfaction of the OG was higher than that of the CG (All $P<0.05$). Conclusion: Prone nursing combined with ECMO can reduce the incidence of complications of severe pneumonia and improve the cardiopulmonary function of patients, which is worthy of clinical promotion.

Keywords: Prone position nursing, extracorporeal membrane oxygenation, severe pneumonia, complications, cardiopulmonary function

Introduction

Pneumonia is a common infectious disease, which affects the airway, alveoli and interstitium. If it is not treated promptly and effectively, it will develop into severe pneumonia and even to acute respiratory distress syndrome (ARDS) [1, 2]. According to statistics, more than 1.5 million adults were hospitalized for community acquired pneumonia (CAP) in the United States, and about 100,000 adults died during hospitalization [3]. Pneumonia is a serious public health problem in the world. Although progress has been made in antimicrobial therapy, pneumonia is still the main cause of death caused by infectious diseases in the world [4]. Therefore, it is particularly important to seek effective treatment and clinical nursing for patients with severe pneumonia.

Extracorporeal membrane oxygenation (ECMO) is an emergency treatment method for patients with severe acute respiratory failure and refractory heart failure [5]. It can effectively correct the symptoms of hypoxia in the whole body tissues and save time for follow-up treatment. Studies by Pappalardo et al. [6] showed that venous-arterial extracorporeal membrane oxygenation (VA-ECMO) improved the oxygenation and peripheral circulation in patients with cardiogenic shock, and improved the prognosis of patients. Kjaergaard et al. [7] showed that EMCO treatment of pulmonary embolism could reduce the risks caused by thrombolytic drugs and save the lives of patients. Hospital mortality rate decreased with the increase of ECMO utilization rate [8]. However, complications such as hemorrhage and infection of puncture site may occur during EMCO treatment [9], thus reducing the therapeutic effect. Therefore, it is of great significance to seek a scientific nursing method to reduce the risks brought by ECMO treatment. Studies have shown that prone position ventilation can improve oxygenation and

survival rate of ARDS patients [10, 11]. At present, there is little research on ECMO treatment combined with supine nursing for severe pneumonia. The incidence of complications in ECMO treatment is relatively high, and the effect of combined treatment is still unclear. This study reported combined use of ECMO treatment and prone position nursing intervention for patients with severe pneumonia, and studied the role of combined treatment on reducing complications and cardiopulmonary function in patients, so as to provide treatment reference for clinic.

Materials and methods

Clinical data of patients

Altogether 96 patients with severe pneumonia diagnosed in Shanghai General Hospital from December 2016 to June 2018 were collected as the research participants. Among them, 48 patients were randomly selected into the observation group (OG) to receive prone position nursing combined with ECMO nursing, and the other 48 patients were selected as the control group (CG) to receive routine nursing combined with ECMO nursing. This study was approved by the Medical Ethics Committee.

Inclusion and exclusion criteria

Inclusion criteria: all patients were treated as severe pneumonia by chest X-ray and laboratory examination, which was in accordance with the 2016 Chinese Medical Association Diagnostic Guidelines for Severe Pneumonia [12]; patients had complete clinical data; patients conformed to ECMO treatment indications; patients and their families have signed informed consent forms.

Exclusion criteria: patients had severe infection in other parts; patients combined with respiratory failure and heart failure, severe liver and kidney function damage, cancer, hematological diseases, mental dysfunction, and communication disorders; lactation and pregnancy patients.

Nursing methods

The CG received routine nursing including vital signs observation, ward environment nursing, anti-inflammatory symptomatic treatment and ECMO nursing.

The OG received prone position nursing combined with ECMO nursing, and the specific contents included: (1) Psychological intervention: timely communication and psychological counseling were applied for patients with anxiety or depression. Furthermore, efficacy and prognosis of the disease were introduced to the patient according to the patient's situation, etiology, and treatment methods, so that the patient could fully understand the disease. The patient's medication was supervised, and the medication and adverse reactions were reminded and recorded. (2) Health education: the hazards of diseases and the importance of prevention, the causes, symptoms, prevention and treatment methods and nursing measures were informed to patients, and the patients' questions were answered patiently. (3) ECMO care: whether each pipe is firmly fixed and whether the elasticity of elastic bandage used on ankle and knee is appropriate were checked carefully. Whether the incubation position on the X-ray film is normal was checked. The temperature of the water box was controlled at 36~37°C to prevent discomfort caused by hypothermia or hyperthermia. The change of the color of the membrane oxygenator was closely observed. If the color deepened and coagulation occurred, the membranous lung should be replaced immediately and the heparin dosage was adjusted according to the actual situation. Dressing should be changed every day at the puncture site. The wound for swelling and bleeding and the changes of the exposed length was observed, so as to avoid vortex or accidental prolapse due to abnormally deep insertion. The flow rate was continuously adjusted according to the cardiopulmonary function of the patient. During the operation of the centrifugal pump, the blood flow rate should be ensured to be stable, and the doctor was needed to be notified immediately if there was any abnormality. Whether the puncture lower limb of the patient has anoxia, stiffness and swelling was checked. Urine volume per hour and vital signs were closely monitored. (4) Prone position nursing: prone position was selected for ECMO treatment. If the patient was able to tolerate the situation, we could try to lower the head and upper the feet, with the face down or lying on the side to keep the trachea unobstructed and easy to observe. Soft pillow was used at the chest, head, leg, hip and abdomen of the patient to

prevent crush injury. Electrocardiogram electrode was changed to the back corresponding to the supine position. Atomization was given during the prone position. Both hands were used to tap the back and mechanical vibration was used to expel phlegm. (5) Complication nursing: whether the wound was infected, red, swell, hot and pain was closely observed. The contaminated dressing was replaced in time, and symptomatic treatment was carried out. The pipeline connection should be firm and be reinforced when necessary to prevent the pipeline from collapsing and air embolism. Analgesic and sedative drugs were used to relieve the pain of the patient, relax the patient and prevent emotional agitation from affecting treatment. Bleeding of the puncture site, excreta and drainage fluid was observed. The occurrence of severe bleeding complications such as intracranial hematoma and systemic hemorrhage was monitored, and invasive puncture or removal of various deep vein catheterization should be avoided to prevent bleeding caused by inadequate hemostasis. Vasodilators was applied to correct hypotension caused by decreased systemic vascular resistance.

Outcome measures

Main outcome measures: the complications of the two groups of patients; cardiopulmonary function before and 7 days after nursing; cardiac function indexes, including left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD) and left ventricular ejection fraction (LVEF); pulmonary function indexes, including forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). The self-made nursing satisfaction questionnaire was applied to evaluate the nursing satisfaction (total satisfaction = satisfaction + basic satisfaction), and the nursing satisfaction of the two groups of patients was observed.

Secondary outcome measures: VAS pain scale was used to evaluate and compare the pain situation of the two groups after nursing for 3 days and 7 days. The point 0 indicates painless, while higher score indicates more severe pain. SAS and SDS scores were used to evaluate and compare the negative emotions of the two groups of patients before and after 7 days of nursing. The total score of SAS/SDS below 50 indicates normal, and the higher score indicates more serious anxiety/depression. The MMAS-8 scale was used to evaluate the compliance of patients.

Statistical analysis

SPSS23 was applied to perform statistical analysis. GraphPad Prism 7 (Graphpad software Co., Ltd., San Diego, USA) was applied to visualize pictures of the collected data. Counting data were represented as usage (%) and analyzed by chi-square, which expressed as χ^2. Measurement data were represented by Meas ± SD. All measurement data were conformed to normal distribution. Independent sample t test was applied for pair-wise comparison, and paired t test for intra-group comparison, both were expressed by t. $P<0.05$ or $P<0.001$ indicates statistically significant.

Results

Comparison of clinical data

By comparing the general clinical data, it was found that there was no statistical difference in age, BMI, gender, APACHE-II score, disease composition, smoking history, drinking history and residence between OG and CG ($P>0.05$) (**Table 1**).

Complications of two groups

Comparing the complications, it was found that there were 3 cases of infection, 2 cases of thrombosis, 2 cases of hemorrhage and 1 case of hypotension in the OG, with a total of 8 cases (16.65%). There were 7 cases of infection, 4 cases of thrombosis, 5 cases of hemorrhage and 4 cases of hypotension in the CG, with a total of 20 cases (33.33%). The complication rate in the OG was evidently lower than that in the CG ($P<0.05$), as shown in **Table 2**.

Comparison of cardiopulmonary function between two groups of patients

By comparing the cardiac function indexes of the two groups of patients, it was found that there was no significant difference in LVEDD (50.31±4.28) (50.47±4.13), LVESD (37.53±4.15) (36.75±3.94) and LVEF (42.17±4.08) (41.68±4.12) between the OG and the CG before nursing ($P>0.05$). After 7 days of nursing, LVEDD (41.86±3.54), LVESD (29.87±3.26)

Table 1. Comparison of clinical data

Factor	OG (n=48)	CG (n=48)	t/χ^2	P
Age (years)	48.6±9.8	50.7±8.4	1.127	0.263
BMI (kg/m^2)	21.8±1.62	22.2±1.65	1.198	0.234
Gender				
Male	27 (56.25)	22 (45.83)	1.042	0.307
Female	21 (43.75)	26 (54.17)		
APACHE-II score	31.28±10.12	34.22±6.78	1.672	0.098
Disease types				
Viral pneumonia	20 (41.67)	23 (47.92)	1.238	0.539
Bacterial pneumonia	17 (35.42)	12 (25.00)		
Mycoplasma pneumonia	11 (22.91)	13 (27.08)		
Smoking history				
Yes	32 (66.67)	38 (79.17)	1.899	0.168
No	16 (33.33)	10 (20.83)		
Drinking history				
Yes	19 (39.58)	22 (45.83)	0.383	0.536
No	29 (60.42)	26 (54.17)		
Residence				
Rural	27 (51.11)	22 (55.56)	1.042	0.307
Urban	21 (48.89)	26 (44.44)		

in the OG were lower than before treatment (P<0.001), LVEF (59.44±4.88) were evidently higher than before treatment (P<0.001), while LVEDD (48.83±5.26), LVESD (35.24±2.57) in the CG had no evident difference compared with before treatment. LVEF (50.42±5.03) was evidently increased (P<0.001). LVEDD and LVESD in the OG were significantly lower than those in the control group (P<0.001), and LVEF was evidently higher than those in the CG (P<0.001), as shown in **Figure 1**.

By comparing the cardiac function indexes, it was found that there was no significant difference in FEV1 (1.27±0.29) (1.30±0.21) and FVC (2.16±0.62) (2.13±0.71) between the OG and the CG before nursing (P>0.05). After 7 days of nursing, both FEV1 and FVC were evidently higher than before nursing (P<0.001). In addition, FEV1 (2.86±0.35) (1.65±0.74) and FVC (3.29±0.57) (2.60±0.45) in the OG were evidently higher than those in the CG (P<0.001), as shown in **Figure 2**.

Comparison of pain

By comparing the VAS scores, it was found that the VAS scores of the OG were evidently lower than those of the CG after 3 days of nursing (P<0.001), and the VAS scores of the OG were evidently lower than those of the CG after 7 days of nursing (P<0.001), as shown in **Table 3**.

Comparison of SAS and SDS score

By comparing the SAS and SDS scores, it was indicated that there was no significant difference of the SAS and SDS scores before nursing. After 7 days of nursing, the SAS and SDS scores were evidently lower than those before nursing (P<0.05), and the SAS and SDS scores of OG were evidently lower than those in the CG (P<0.001), as shown in **Table 4**.

Comparison of treatment compliance

The compliance was evaluated by MMAS scale score. The results showed that the MMAS-8 score in the OG (5.81±1.05) was evidently higher than that in the CG (5.16±0.78) (P< 0.001), as shown in **Figure 3**.

Comparison of nursing satisfaction

After nursing intervention, the OG was satisfied with the nursing in 16 cases, basically satisfied in 26 cases and unsatisfied in 6 cases, with a total satisfaction rate of 87.5%. In the CG, 10 cases were satisfied with the nursing, 24 cases were basically satisfied, 14 cases were unsatisfied, and the total satisfaction rate of nursing was 70.83%. The total satisfaction of nursing in the OG was evidently higher than that in the CG (P<0.05), as shown in **Table 5**.

Discussion

Severe pneumonia is a common clinical critical disease. The prognosis of patients with severe pneumonia is poor, and the mortality rate reaches 30%~50% [13]. ECMO is an important cardiopulmonary support technology, and is the final treatment method when conventional treatment of heart failure and lung failure is ineffective. ECMO enables the body to temporarily replace lung function and part of heart function through external gas exchange, and

Table 2. Comparison of complications

Group	Infection	Thrombus	Hemorrhage	Hypotension	Total
Observation group (n=48)	3 (6.25)	2 (4.16)	2 (4.16)	1 (2.08)	8 (16.65)
Control group (n=48)	7 (14.58)	4 (8.33)	5 (10.42)	4 (8.33)	20 (33.33)
χ^2					7.261
P					0.007

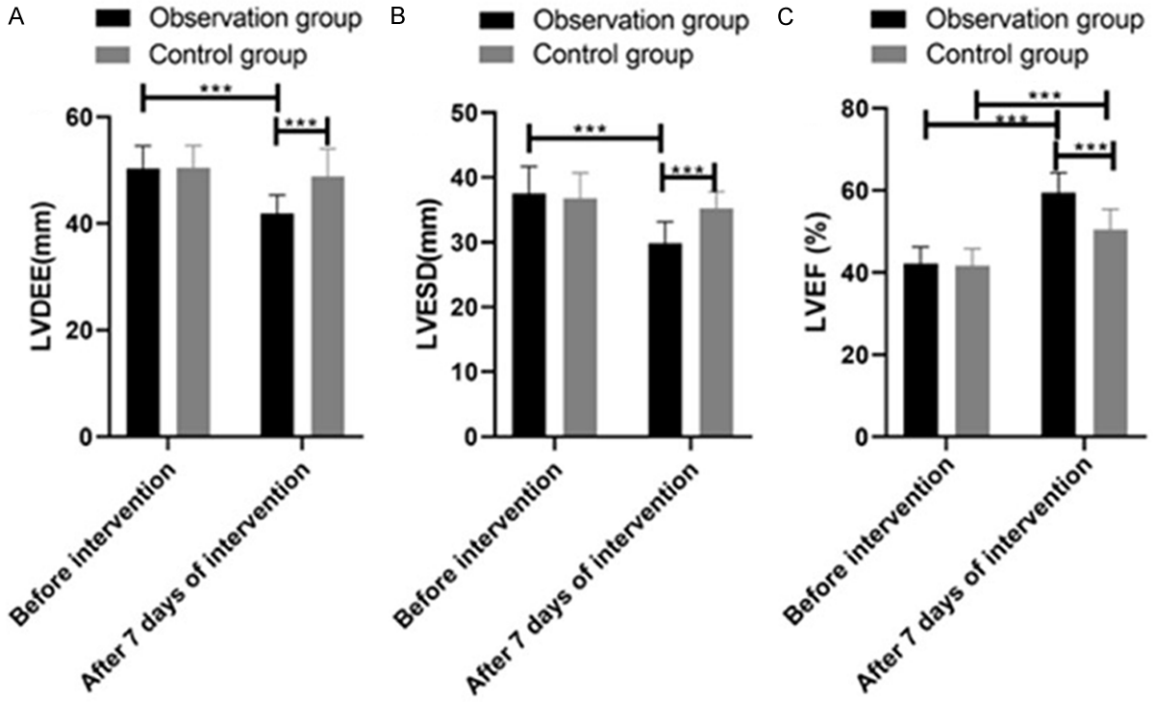

Figure 1. Comparison of cardiac function between two groups of patients. A. Before nursing, there was no significant difference in LVEDD between the two groups. After 7 days of nursing, LVEDD in the observation group was significantly lower than that before nursing, while there was no significant difference in the control group. LVEDD in the observation group was significantly lower than that in the control group. B. There was no significant difference in LVESD between the two groups before nursing. After 7 days of nursing, LVESD in the observation group was significantly lower than that before nursing, while there was no significant difference in the control group. LVESD in the observation group was significantly lower than that in the control group. C. There was no significant difference in LVEF between the two groups before nursing. After 7 days of nursing, LVEDD in the two groups was significantly higher than that before nursing, and LVEF in the observation group was significantly higher than that in the control group. ***indicates P<0.001.

can strive for recovery of respiratory or heart function to save time for subsequent treatment [14]. As adequate oxygenation requires a large cannula inserted through femoral vessels, this process may lead to severe limb ischemia [15], while reports also indicate that excessive heparin use may lead to hemorrhage [16], thrombosis, infection, renal failure and neurological complications in ECMO therapy [17, 18]. Therefore, it is of great significance to seek an effective nursing method to prevent complications during ECMO treatment. Prone position is considered to be one of the most effective treatments for patients with ARDS. It provides more even ventilation to improve oxygenation and remove carbon dioxide [19]. Therefore, this study will explore the effect of prone position nursing combined with ECMO on preventing complications and improving cardiopulmonary function in patients with severe pneumonia.

In this study, patients in the OG were treated with prone position nursing combined with ECMO intervention, while patients in the CG were treated with routine nursing combined

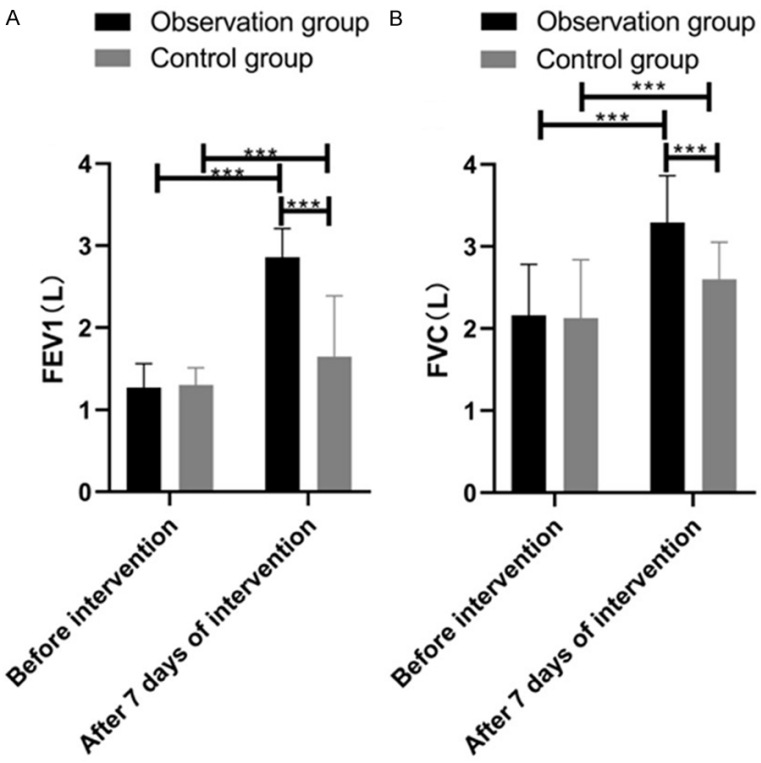

Figure 2. Comparison of lung function between two groups of patients. A. There was no significant difference in FEV1 between the two groups before nursing. FEV1 in the two groups after 7 days of nursing was significantly higher than before nursing, and the patients in the observation group were significantly higher than that in the control group. B. There was no significant difference in FVC between the two groups before nursing. FVC in the two groups after 7 days of nursing was significantly higher than before nursing, and the patients in the observation group were significantly higher than that in the control group. ***indicates P<0.001.

Table 3. Comparison of VAS score

Group	After 3 days of nursing	After 7 days of nursing
Observation group (n=48)	5.31±0.75	1.74±0.45
Control group (n=48)	6.44±0.88	3.48±0.89
t	6.771	12.09
P	<0.001	<0.001

with ECMO intervention. We made statistics on the complications within 7 days of intervention. The results showed that both groups of patients had infection, thrombosis, hemorrhage and hypotension, but the total complications in the OG was evidently lower than that in the CG. Then we compared the cardiopulmonary function of the two groups of patients after nursing. The results showed that the improvement degree of the cardiopulmonary function in the OG was higher than that in the CG, indicating that prone position nursing could significantly reduce the incidence of complications during ECMO treatment, improve the cardiopulmonary function and the therapeutic effect of ECMO. Prone position ventilation during ECMO treatment could effectively increase ventilation on the back side of lung tissue, strengthen alveolar ventilation function, improve oxygenation, and reduce the occurrence of ventilator-associated pneumonia and lung injury [20, 21]. This was also confirmed by the improvement of cardiopulmonary function of patients in OG through prone position nursing in our study. Prone position ventilation can improve oxygenation, but there is a risk of complications related to pipelines when changing body position [22]. We have taken targeted measures against possible complications of ECMO treatment, the steps were as follows: timely replacement of wound dressings and reinforcement of pipelines were applied, invasive puncture or removal of various deep vein catheterization was avoided, the occurrence of serious bleeding complications such as puncture site, intracranial hematoma and systemic hemorrhage was observed, vasodilators were applied to improve hypotension. The research results showed the superiority of combined intervention to prevent complications. He et al. [23] analyzed a case of pneumonia complicated with pneumothorax due to severe drug resistance, which was successfully treated by ECMO combined with prone position high frequency oscillatory ventilation. Otterspoor et al. [24] also showed that patients with H1N1 pneumonia complicated with invasive aspergillosis could finally recover completely by applying prone position combined with ECMO. Moore [25] and Ghelichkhani [26] et al. have shown that prone position ventilation, as an adjuvant therapy, can enhance the

Table 4. Comparison of SAS and SDS scores

Group	SAS		SDS	
	Before nursing	After 7 days of nursing	Before nursing	After 7 days of nursing
Observation group (n=48)	68.63±4.25	43.16±3.21*	64.28±4.35	39.24±3.61*
Control group (n=48)	69.77±4.18	49.79±4.16*	65.78±3.96	46.58±4.08*
t	1.325	8.742	1.767	9.335
P	0.188	<0.001	0.081	<0.001

*indicates that there is a statistical difference compared with that before nursing.

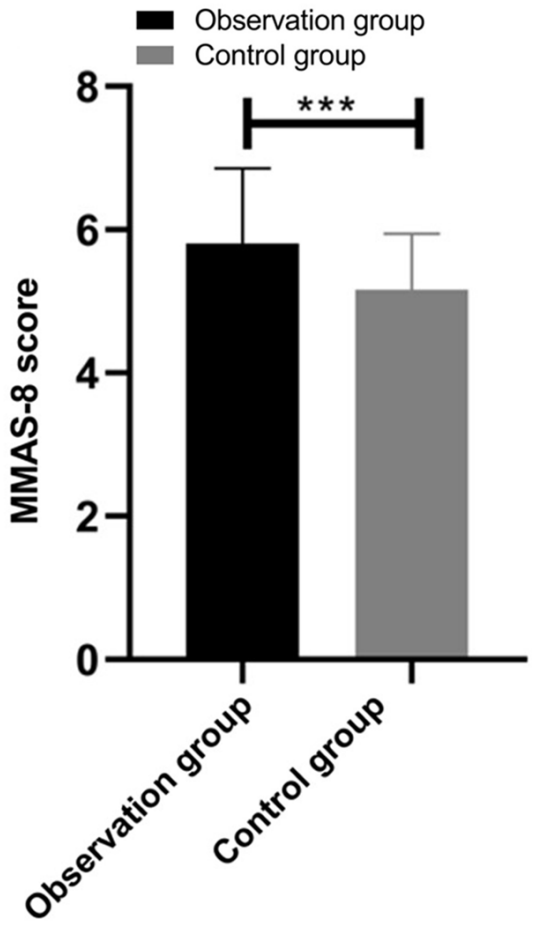

Figure 3. Comparison of MMAS-8 scores between the two groups. The MMAS-8 scores in the observation group were significantly higher than those in the control group, ***indicates P<0.01.

oxygenation level of COVID-19 infected patients, reduce the occurrence of complications such as pressure sores and pulmonary edema, and improve the quality of life of patients. This is similar to our research results, which further confirms the effect of prone position combined with ECMO and its effect on preventing complications, and is worthy of clinical application.

Pain is a common symptom of ECMO treatment. Severe pneumonia is in critical condition, and negative emotions caused by the disease and treatment often occur [27]. The patients in the OG were treated with analgesic and sedative drugs combined with psychological intervention. The results showed that the pain situation of OG was evidently reduced, the negative emotions were alleviated, and the psychological intervention in the prone position nursing combined with ECMO intervention mode in this study acted in improving the negative emotions of the patients. The patient's treatment compliance is very important for the patient's recovery. Poor compliance behavior will affect the patient's therapeutic effect and postoperative improvement [28], so improving the patient's compliance is the key to recovery. Many patients are suffered from psychological burden due to lack of understanding of the disease, and the compliance is low due to lack of understanding of the treatment plan [29]. Then we counted the patient's compliance with treatment, and it was revealed that the compliance of OG was evidently higher than that of CG. We speculated that the patients had confidence in treatment after psychological intervention in this study, while health education for patients deepened the patient's understanding of the disease and treatment methods, thus improving compliance. At the end of the study, the patient's nursing satisfaction was investigated. The investigation results showed that the OG was evidently higher than that of the CG, which indicated that the nursing method of OG could improve the patient's nursing satisfaction. The patients were easy to accept the treatment and had high recognition, which provided a strong basis for the application and promotion of prone position combined with ECMO intervention in the clinical application of severe pneumonia.

Table 5. Comparison of nursing satisfaction

Group	OG (n=48)	CG (n=48)	χ^2	P
Satisfied	16 (33.33)	10 (20.83)	1.899	0.168
Basic satisfied	26 (54.17)	24 (50.00)	0.167	0.409
Unsatisfied	6 (12.50)	14 (29.17)	4.042	0.044
Total satisfaction	42 (87.50)	34 (70.83)		

Although this study confirmed that prone position combined with ECMO intervention had better benefits in severe pneumonia, there are still some deficiencies. For example, we have not investigated the quality of life of patients. What's more, we have not conducted follow-up investigation on the survival of the patients. These deficiencies will be supplemented and improved in future studies.

To sum up, prone position nursing combined with ECMO intervention can reduce the incidence of complications of severe pneumonia and improve patients' cardiopulmonary function, which is worthy of clinical application.

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Disclosure of conflict of interest

None.

Address correspondence to: Yu Bai, 2A ICU, Shanghai General Hospital, 650th New Songjiang Road, Shanghai 201620, China. Tel: +86-185-01702808; E-mail: 18121288390@126.com

References

[1] Chahin A and Opal SM. Severe pneumonia caused by legionella pneumophila: differential diagnosis and therapeutic considerations. Infect Dis Clin North Am 2017; 31: 111-121.

[2] Chen C, Shi L, Li Y, Wang X and Yang S. Disease-specific dynamic biomarkers selected by integrating inflammatory mediators with clinical informatics in ARDS patients with severe pneumonia. Cell Biol Toxicol 2016; 32: 169-184.

[3] Ramirez JA, Wiemken TL, Peyrani P, Arnold FW, Kelley R, Mattingly WA, Nakamatsu R, Pena S, Guinn BE, Furmanek SP, Persaud AK, Raghuram A, Fernandez F, Beavin L, Bosson R, Fernandez-Botran R, Cavallazzi R, Bordon J, Valdivieso C, Schulte J and Carrico RM. Adults hospitalized with pneumonia in the United States: incidence, epidemiology, and mortality. Clin Infect Dis 2017; 65: 1806-1812.

[4] Cilloniz C, Martin-Loeches I, Garcia-Vidal C, San Jose A and Torres A. Microbial etiology of pneumonia: epidemiology, diagnosis and resistance patterns. Int J Mol Sci 2016; 17: 2120.

[5] Rao P, Khalpey Z, Smith R, Burkhoff D and Kociol RD. Venoarterial extracorporeal membrane oxygenation for cardiogenic shock and cardiac arrest. Circ Heart Fail 2018; 11: e004905.

[6] Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G, Greco T, Lembo R, Müllerleile K, Colombo A, Sydow K, De Bonis M, Wagner F, Reichenspurner H, Blankenberg S, Zangrillo A and Westermann D. Concomitant implantation of Impella(®) on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. Eur J Heart Fail 2017; 19: 404-412.

[7] Kjaergaard B, Kristensen JH, Sindby JE, de Neergaard S and Rasmussen BS. Extracorporeal membrane oxygenation in life-threatening massive pulmonary embolism. Perfusion 2019; 34: 467-474.

[8] Karagiannidis C, Brodie D, Strassmann S, Stoelben E, Philipp A, Bein T, Müller T and Windisch W. Extracorporeal membrane oxygenation: evolving epidemiology and mortality. Intensive Care Med 2016; 42: 889-896.

[9] Mi MY, Matthay MA and Morris AH. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med 2018; 379: 884-887.

[10] Scholten EL, Beitler JR, Prisk GK and Malhotra A. Treatment of ARDS with prone positioning. Chest 2017; 151: 215-224.

[11] Trick WE, Sokalski SJ, Johnson S, Bunnell KL, Levato J, Ray MJ and Weinstein RA. Effectiveness of probiotic for primary prevention of clostridium difficile infection: a single-center before-and-after quality improvement intervention at a tertiary-care medical center. Infect Control Hosp Epidemiol 2018; 39: 765-770.

[12] Cao B, Huang Y, She DY, Cheng QJ, Fan H, Tian XL, Xu JF, Zhang J, Chen Y, Shen N, Wang H, Jiang M, Zhang XY, Shi Y, He B, He LX, Liu YN and Qu JM. Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. Clin Respir J 2018; 12: 1320-1360.

[13] Wang L and Song Y. Efficacy of zinc given as an adjunct to the treatment of severe pneumonia: a meta-analysis of randomized, double-blind and placebo-controlled trials. Clin Respir J 2018; 12: 857-864.
[14] Rambaud J, Guilbert J, Guellec I, Jean S, Durandy A, Demoulin M, Amblard A, Carbajal R and Leger PL. Extracorporeal membrane oxygenation in critically ill neonates and children. Arch Pediatr 2017; 24: 578-586.
[15] Lamb KM, DiMuzio PJ, Johnson A, Batista P, Moudgill N, McCullough M, Eisenberg JA, Hirose H and Cavarocchi NC. Arterial protocol including prophylactic distal perfusion catheter decreases limb ischemia complications in patients undergoing extracorporeal membrane oxygenation. J Vasc Surg 2017; 65: 1074-1079.
[16] Thomas J, Kostousov V and Teruya J. Bleeding and thrombotic complications in the use of extracorporeal membrane oxygenation. Semin Thromb Hemost 2018; 44: 20-29.
[17] Biffi S, Di Bella S, Scaravilli V, Peri AM, Grasselli G, Alagna L, Pesenti A and Gori A. Infections during extracorporeal membrane oxygenation: epidemiology, risk factors, pathogenesis and prevention. Int J Antimicrob Agents 2017; 50: 9-16.
[18] Lorusso R, Barili F, Mauro MD, Gelsomino S, Parise O, Rycus PT, Maessen J, Mueller T, Muellenbach R, Belohlavek J, Peek G, Combes A, Frenckner B, Pesenti A and Thiagarajan RR. In-hospital neurologic complications in adult patients undergoing venoarterial extracorporeal membrane oxygenation: results from the extracorporeal life support organization registry. Crit Care Med 2016; 44: e964-972.
[19] Gattinoni L, Busana M, Giosa L, Macrì MM and Quintel M. Prone positioning in acute respiratory distress syndrome. Semin Respir Crit Care Med 2019; 40: 94-100.
[20] Pelosi P, Brazzi L and Gattinoni L. Prone position in acute respiratory distress syndrome. Eur Respir J 2002; 20: 1017-1028.
[21] Gattinoni L, Taccone P, Carlesso E and Marini JJ. Prone position in acute respiratory distress syndrome. Rationale, indications, and limits. Am J Respir Crit Care Med 2013; 188: 1286-1293.
[22] Masuda Y, Tatsumi H, Imaizumi H, Gotoh K, Yoshida S, Chihara S, Takahashi K and Yamakage M. Effect of prone positioning on cannula function and impaired oxygenation during extracorporeal circulation. J Artif Organs 2014; 17: 106-109.
[23] He H, Wang H, Li X, Tang X, Wang R, Sun B and Tong Z. Successful rescue combination of extracorporeal membrane oxygenation, high-frequency oscillatory ventilation and prone positioning for the management of severe methicillin-resistant Staphylococcus aureus pneumonia complicated by pneumothorax: a case report and literature review. BMC Pulm Med 2017; 17: 103.
[24] Otterspoor LC, Smit FH, van Laar TJ, Kesecioglu J and van Dijk D. Prolonged use of extracorporeal membrane oxygenation combined with prone positioning in patients with acute respiratory distress syndrome and invasive Aspergillosis. Perfusion 2012; 27: 335-337.
[25] Moore Z, Patton D, Avsar P, McEvoy NL, Curley G, Budri A, Nugent L, Walsh S and O'Connor T. Prevention of pressure ulcers among individuals cared for in the prone position: lessons for the COVID-19 emergency. J Wound Care 2020; 29: 312-320.
[26] Ghelichkhani P and Esmaeili M. Prone position in management of COVID-19 patients; a commentary. Arch Acad Emerg Med 2020; 8: e48.
[27] Maruyama T, Gabazza EC, Morser J, Takagi T, D'Alessandro-Gabazza C, Hirohata S, Nakayama S, Ramirez AY, Fujiwara A, Naito M, Nishikubo K, Yuda H, Yoshida M, Takei Y and Taguchi O. Community-acquired pneumonia and nursing home-acquired pneumonia in the very elderly patients. Respir Med 2010; 104: 584-592.
[28] Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C and Haynes RB. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2014; 2014: CD000011.
[29] Heydari A, Ziaee ES and Gazrani A. Relationship between awareness of disease and adherence to therapeutic regimen among cardiac patients. Int J Community Based Nurs Midwifery 2015; 3: 23-30.