Effect of The FOCUS Program on The Self-Efficacy of Caregivers for Patients With Advanced Lung Cancer

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Research Article

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Abstract

Objective To investigate the effect of the FOCUS program on the self-efficacy of caregivers of patients with advanced lung cancer.

Method In this experimental study, a total of 108 caregivers for patients admitted to a tertiary comprehensive hospital from April 2019 to December 2019 were recruited based on inclusion and exclusion criteria. Based on their admission dates, the caregivers were divided into a control group (54 cases), which only completed routine measures, and a test group (54 cases), which completed the FOCUS Program in addition to routine measures. At the 4th week of the intervention, general self-efficacy, caregiving burden, coping styles and mood states were compared between the control group and the test group.

Results The general self-efficacy scale, caregiver burden scale, simple coping style scale and mood state scale were compared between the two groups at the 4th week of the intervention and at 8 weeks after the intervention.

After the intervention, the self-efficacy scores of the test group (24.37 ± 4.375) were higher than those of the control group (17.50 ± 3.479), and the difference was statistically significant ($t = -9.032$, $P < 0.05$); the caregiving burden scores of the test group (41.65 ± 2.735) were lower than those of the control group (47.33 ± 7.066), and the difference was statistically significant ($t = 5.514$, $P < 0.05$); the coping style scores of the experimental group (33.20 ± 5.533) were significantly higher than those of the control group (28.76 ± 3.420) ($t = -5.021$, $P < 0.05$); the mood state scale scores of the test group (106.17 ± 12.400) were lower than those of the control group (127.65 ± 11.754), and the difference was statistically significant ($t = 9.239$, $P < 0.05$).

The results showed that the intergroup comparisons, group comparisons and interactions were statistically significant ($P < 0.05$).

Conclusion The FOCUS Program can effectively improve the self-efficacy of caregivers, reduce their caregiving burden improve their coping styles and enhance their mood states.

Introduction

Self-efficacy is a person's belief in his or her ability to accomplish a specific task under different circumstances^[1]. China has a large population and a relative lack of medical resources, so caregivers are the main force of family care services. A high or low level of self-efficacy among caregivers will directly affect the caregivers' ability to care, which is related to whether they can provide good care for patients^[2-3]. Research has shown that self-efficacy can help caregivers cope with caregiving stress and is considered a positive factor in health and quality of life^[4]. At present, research on the self-efficacy of patients with advanced cancer in China is still in its infancy, and a number of foreign studies have proven the role of the FOCUS program in improving the self-efficacy of cancer patients' caregivers^[5-6]. The FOCUS program (family involvement, optimistic attitude, coping effectiveness, uncertainty reduction, and symptom management) is an evidence-based psychological education intervention^[7]. The purpose of this study is to provide a clinical

reference for the application of the FOCUS program in China by developing a Chinese version of the program to provide interventions for caregivers of patients with advanced lung cancer.

Subjects And Methods

1.1 Subjects

A total of 108 caregivers of patients with advanced lung cancer who were hospitalized in a tertiary general hospital from April 2019 to December 2019 were selected (caregivers could only be included once, even if patients had repeated hospitalizations). The caregivers included from April 2019 to August 2019 composed the control group, and the test group comprised caregivers included from September 2019 to December 2019. The control group received routine nursing care, and the experimental group completed the FOCUS program. The inclusion criteria were as follows: caregivers of patients diagnosed with cancer by pathology or cytology, with tumor-bearing survival and TNM clinical stage IV advanced lung cancer; the expected survival of patients with advanced lung cancer is greater than 6 months; the caregivers in this study performed most of the care activities; age ≥ 18 years old; the patient's cancer status was known; willing to participate and able to communicate normally; simple word recognition ability; able to read or understand the contents of the scale; sane and able to cooperate; provided informed consent.

1.2 Research Methods

1.2.1 Preliminary arrangement of the intervention plan

In this study, the FOCUS program management scheme developed by Professors Titler M G^[8] and Fatemeh Moghaddam Tabrizi^[9] from the United States was quoted. The main content includes five parts: family involvement, optimism, coping effectiveness, uncertainty reduction and symptom management. The original scheme, structure, and meaning of the intervention remained unchanged while it was adapted to the characteristics of China's population. During this process, seven experts from the tertiary general hospital were consulted for guidance, including two experts on the diagnosis and treatment of malignant tumors, three nursing experts, 1 national psychological consultant, and 1 nursing research expert. See supplementary Table 1

1.2. 2 Pretest

To explore the feasibility and scientific nature of the intervention strategy, further discover practical problems and improve the intervention plan, 4 caregivers of advanced lung cancer patients who agreed to participate in this study and met the inclusion criteria were selected for the pretest. The final intervention plan was formed by modifying the intervention plan based on the feedback of the pretest intervention subjects and expert opinions. See supplementary Table 2—See supplementary Table 3—See supplementary Table 4—See supplementary Table 5

1.2.3 The FOCUS program has been officially revised

Combined with the needs of the research, the formulation process of the program includes preliminary formulation, pretest, expert consultation, program modification and formal program establishment. The intervention plan was modified based on the feedback of pretrial intervention subjects and expert opinions. For example, video, audio and symptom management can be converted into QR codes, which can be sent by mobile phones. Caregivers were encouraged to create a psychological pressure relief wall, display the effect of handicrafts on the psychological pressure relief wall, and write their hopes, wishes and blessings on the handmade work. Caregivers decided whether they were willing to share. Finally, an intervention plan was formed, as detailed in supplementary Table 6.

1.2.4 Intervention methods in the test group

The FOCUS program lasted for 4 weeks. The intervention process is as follows:

- (1) When the caregivers accompanied the patients to the hospital for the first time, the caregivers provided general data and completed a questionnaire related to the research indicators before the intervention. Then, according to the needs of the research subjects, the researchers were assigned a day in the subsequent 4 weeks to be interviewed for 15-20 minutes according to the intervention plan. The researchers recorded patients expressing gratitude to their caregivers.
- (2) Help families maintain an optimistic attitude, carry out handicrafts, and encourage recording and sharing for 15-20 mins once a week for a total of 4 weeks. In the process of development, the handicrafts were displayed on the pressure reduction wall if the caregivers gave permission.
- (3) Conduct lifestyle intervention for caregivers as planned and encourage patients to engage in appropriate exercise. Exercises such as walking and brisk walking should occur 3 times a week for 4 weeks, with at least 15 min per session. Weekly telephone and network supervision should also occur.
- (4) Based on the caregivers' leisure time, researchers and caregivers go to the classroom together to watch the road to cancer and talk about life and death or sadness; alternatively, the QR code is sent to the caregivers phones, and they are reminded to watch the video during the week for 40-60 min each weeks.
- (5) According to the needs of caregivers, corresponding symptom management cards should be provided. Push QR code for symptom management. Health care personnel should regularly communicate with caregivers (face-to-face or online) on any day of the week for 4 weeks, with a health instruction time of 10 min/time.

1.2.5 Intervention method for control group

The control group of caregivers underwent routine care in accordance with the internal medicine nursing care requirements for patients with lung cancer. Patients were followed at the center, a warm atmosphere is fostered for patients and caregivers in the hospital environment, the trust of patients and caregivers is cultivated, timely to caregivers make related nursing health guidance to lung diseases including conventional drugs, life nursing guidance to patients with lung cancer, pain, rehabilitation, patients with the

guidance of daily activities, diet instruction, psychological adjustment guidance and discharge guidance, etc.

1.2.6 Survey tools

1.2.6.1 Questionnaire for general information

The questionnaire was designed by researchers through a literature review and group discussion. The content is divided into two parts. The first part includes demographic and sociological data, including name, gender, age, etc. the second part includes treatment-related information, medical insurance mode, the patient's current situation, etc.

1.2.6.2 General self-efficacy scale-Schwarzer (GSEs)^[10]

Zhang developed this scale, which includes 10 items. Responses are provided using a 4-point Likert scale ranging from 1 ~ 4 ("completely incorrect" ~ "completely correct"); the total score ranges from 10 to 40 points, such that higher scores indicate higher levels of self-efficacy. Cronbach's α coefficient for this scale was 0.84.

1.2.6.3 Caregiver Burden Interview Scale (Zarit Caregiver Burden Interview, ZBI)^[11]

The ZBI was developed by Zarit et al. and translated into Chinese by Wang Lie et al. in 2006. The Cronbach's α for the Chinese version of the ZBI was 0.87. Items are scored using a 5-point Likert scale ranging from 0-4 ("none" to "always"), and total scores range from 0-88. Higher scores indicate a heavier level of caregiver burden. This scale has been widely adopted in China.

1.2.6.4 Simplified Coping Style Questionnaire (SCSQ)^[12]

This questionnaire was developed by Xie Yaning and other scholars in 1998. It mainly evaluates the attitudes and practices adopted by individuals when they suffer difficulties or setbacks. The questionnaire includes 20 items across two dimensions: positive coping and negative coping. Items 1 to 12 assess positive coping, and items 13 to 20 assess negative coping. Items are scored on a 4-point scale ranging from 0 (not used) to 3 (frequently used), and total scores range from 0-60. The Cronbach's α coefficient for the scale was 0.90.

1.2.6.5 Poms Cprofile of Mood Ststes (POMS)^[13]

McNair et al. (1971) developed a self-report questionnaire to assess a respondent's mood. In 1995, the Chinese version of the questionnaire was developed by Professor Zhu Baili in China. Its reliability ranged from 0.60 to 0.82, with an average of 0.71, indicating a high level of reliability. The scale consists of 40 items to assess 7 emotions. Each item is scored on a scale ranging from 0 to 4, representing "hardly" to "very much", and the total score ranges from 0 to 136. TMD represents the overall score for emotional disarray, and higher scores indicate worse mental health.

1.2.7 Data collection method

Questionnaires were administered by individuals who were not associated with the intervention, and the researchers underwent unified training to ensure the scientific, normative and accurate collection of questionnaires. Data were only analyzed from subjects who met the inclusion criteria and provided informed consent. The questionnaire was administered before the intervention, at the 4th week of the intervention, and 8 week after the intervention. The questionnaires were administered after the caregivers signed the informed consent form. One-on-one guidance was given. The time to complete the scale was approximately 20 minutes. For those who could not completed the questionnaires alone due to special circumstances, the researcher read the questionnaire and assisted the respondent without guidance. A total of 108 effective questionnaires were collected at the end of the intervention, including 54 in the experimental group and 54 in the control group. The effective rate of the samples was 100%. The overall compliance of the subjects was good.

1.2.8 Statistical methods

Statistical analyses was conducted using SPSS 19.0 statistical software. Data such as age, general self-efficacy, caregiver burden, simple coping style, and state of mind were found to be normally distributed. These data were represented as means±standard deviations and analyzed using repeated-measures analysis of variance and independent samples t-test; the Mann-Whitney U test was used to analyze nonnormal data. Categorical data, such as gender, ethnicity and marital status, were expressed as frequencies and percentages. The chi-square test was used to comparison these data between groups. P<0.05 was considered to be statistically significant.

Results

2.1 General data of the subjects

The general information of the two groups of caregivers was comparable, as shown in Table 1.

Table 1 Comparison of general information between the two groups of caregivers (±s)

General information	Control group (N=54)	Test group (N=54)	T/χ^2	P
age	57.63 + / - 12.978	58.22 + / - 11.341	0.253	0.801
gender			0.343	0.558
male	24 (44.4%).	21 (38.9%).		
female	30 (55.6%)	33 (61.1%).		
national			1.009	0.315
Han	53 (98.1%).	54 (100%).		
Ethnic minorities	1 (1.9%).	0 (0.0%)		
Marital status			1.375	0.241
Married	52 (96.3%).	49 (90.7%).		
Unmarried (divorced, widowed, unmarried)	2 (3.7%).	5 (9.3%)		
Number of children			0.244	0.885
childless	4 (7.4%)	5 (9.8%)		
1	32 (59.3%).	33 (61.1%).		
Two or more	18 (33.3%).	16 (29.6)		
Level of education			2.922	0.571
Primary school	22 (40.7%).	24 (44.4%).		
Junior high school	17 (31.5%).	10 (18.5%)		
High school	8 (14.8%)	9 (16.7%)		
college	3 (5.6%)	4 (7.4%)		
University and above	4 (7.4%)	7 (13.0%)		
Working status			1.481	0.477
retired	34 (63.0%).	31 (57.4%).		
work	16 (29.6%).	21 (38.9%).		
unemployment	4 (7.4%)	2 (3.7%).		
Monthly income			4.234	0.237
1000 of below	9 (16.7%)	5 (9.3%)		
1000-3000.	24 (44.4%).	31 (57.4%).		
3000-5000.	18 (33.3%).	12 (22.2%).		

More than 5000	3 (5.6%)	4 (11.1%)		
Religious			0.052	0.820
Yes	13 (24.1%).	12 (22.2%).		
No	41 (75.9%).	42 (77.8%).		
Interests and hobbies			0.172	0.679
Yes	36 (66.7%).	38 (70.4%).		
No				
Self-health status			1.938	0.379
good	19 (35.2%).	19 (35.2%).		
general	34 (63.0%).	31 (57.4%).		
poor	1 (1.8%).	4 (7.4%)		
very poor	0 (0.0%)	0 (0.0%)		
Take care of the time	40 (74.1%).	38 (70.4%).	0.658	0.720
> 6 months	7 (13.0%)	10 (18.5%)		
1-6 months	7 (13.0%)	6 (11.1%)		
< 1 month				
Whether to care full-time or not	37 (68.5%)	36 (66.7%).	0.042	0.837
Yes	17 (31.5%).	18 (33.3%).		
No				
Relationship with the patient			5.796	0.122
spouse	41 (75.9%).	34 (63.0%).		
children	13 (24.1%).	15 (27.8%).		
parents	0 (0.0%)	1 (1.9%).		
Other relative	0 (0.0%)	4 (7.3%)		
Medical payment method for patients			2.621	0.270
Agricultural insurance	32 (59.3%).	26 (48.1%).		
Health care	21 (38.9%).	28 (51.9%).		
At one's own expense	1 (1.8%).	0 (0.0%)		
Health status of the patient			1.887	0.596
good	4 (7.4%)	7 (13.0%)		

general	24 (44.4%).	20 (37.0%).
poor	20 (37.0%).	18 (33.3%).
very poor	6 (11.2%)	9 (16.7%)

2.2 Comparison of general self-efficacy between the two groups

See Table 2 and supplementary Figure 1 for details.

Table 2 Comparison of general self-efficacy scores between the two groups of caregivers

grouping	Before the intervention	At 4 weeks of intervention	8-week follow-up	F _{group}	F _{time}	F _{time*group}
The control group	16.74±4.199	17.50±3.479	18.74±3.707	109.214*	74.578*	68.81*
Experimental group	17.19±3.876	24.37±4.375	29.61±5.314			
T	-0.572	-9.032	-12.328			
P	0.569	0.000	0.000			

Note: *P<0.05

2.3 Comparison of caregiver burden between the two groups

See Table 3 and supplementary Figure 2 for details.

Table 3 Comparison of the caregiver burden scores between of the two groups of caregivers

grouping	Before the intervention	At 4 weeks of intervention	8-week follow-up	F _{group}	F _{time}	F _{time*group}
The control group	49.50±7.432	47.33±7.066	47.48±8.056	25.868*	34.736*	16.097*
Experimental group	49.87±9.546	41.65±2.735	37.04±4.758			
T	-0.225	5.514	8.203			
P	0.822	0.000	0.000			

Note: *P<0.05

2.4 Comparison of simple coping styles between the two groups

See Table 4 and supplementary Figure 3 for details.

Table 4 Comparison of coping style scores between the two groups of caregivers

grouping	Before the intervention	At 4 weeks of intervention	8-week follow-up	F _{group}	F _{time}	F _{time*group}
The control group	28.78±3.780	28.76±3.420	27.57±3.854	32.007*	10.007*	15.751*
Experimental group	28.78±7.000	33.20±5.533	35.39±6.221			
T	0.000	-5.021	-7.848			
P	1.000	0.000	0.000			

Note: *P≤0.05

2.5 Comparison of mood states between the two groups

See Table 5 and supplementary Figure 4 for details.

Table 5 Comparison of mood state scores between the two groups of caregivers

grouping	Before the intervention	At 4 weeks of intervention	8-week follow-up	F _{group}	F _{time}	F _{time*group}
The control group	130.06±14.345	127.65±11.754	124.46±10.876	53.191*	52.085*	26.311*
Experimental group	130.07±17.451	106.17±12.400	105.65±20.507			
T	-0.006	9.239	5.956			
P	0.995	0.000	0.000			

Note: *P≤0.05

Discussion

3.1 FOCUS program improves the self-efficacy of caregivers of patients with advanced lung cancer

This study showed that there was no statistically significant difference in the level of general self-efficacy between the two groups at baseline (P>0.05). At the 4th week of the intervention, the general self-efficacy level of the experimental group (24.37±4.375) was higher than that of the control group (17.50±3.479), After 8 weeks of follow-up, the general self-efficacy score of the study group (29.61±5.314) was still higher than that of the control group (18.74±3.707), All of them were statistically significant (P < 0.05). This indicates that over time, the self-efficacy scores of the two groups of caregivers gradually increase. Furthermore, the rate of increase in the experimental group is significantly higher than that in the control group, indicating

that the self-efficacy level of caregivers will improve over time. Therefore, the self-efficacy level of caregivers of patients with advanced lung cancer can be improved through the focus program.

Studies have shown that caregivers' self-efficacy is influenced by mutual communication^[14-15]. Norton S A and other scholars also pointed out in their studies that sincere communication between patients and caregivers can reduce the burden of caregivers^[16]. Paper cutting, paper cranes and Chinese knots are commonly used images in Eastern culture. In Chinese culture, paper cranes and Chinese knots represent hope, unity, happiness and peace, thus expressing people's pursuit of and prayers for spiritual peace^[17]. Making exquisite handicrafts for other people represents an understanding and desire for life and is a way to express recognition of the values of traditional Chinese culture. Regarding physiological stimulation, handmaking crafts also stimulates abstract thinking and image thinking mechanisms in the brain and results in material creation activities in three-dimensional space^[18]. In this study, caregivers of patients with advanced cancer were asked to handmake crafts. In the process of handcrafting, caregivers' thoughts can be removed from their worries, their psychological anxiety can be adjusted, and their inner blessings and hopes can also be expressed. This is consistent with the research of Agarwal et al^[19]. Proper exercise can not only increase hemoglobin levels in the body and heart output and increase blood oxygen content but also stimulate the pituitary gland to release β -endorphin and enhance the body's tolerance to stimulation, thus effectively relieving the stress of caregivers and improving self-efficacy^[20]. This study encourages caregivers to adopt simple and familiar exercise methods, follow their normal lifestyle, and take advantage of individualization, safety, strong operability and strong promotion. This is consistent with the research of Han Mengfei and Wei Qiang et al^[21-22]. This study provides sound/video: "the power of grief", "the road to cancer", "talk about life and death", in case of selection of matching, vividness, authenticity and thoughtful principles^[23]. Previous research has shown that individuals have the ability to overcome difficulties and grow^[24-25]. Symptom management programs emphasize the mobilization of caregivers' self-efficacy, conform to the ecological instantaneous assessment method, assess caregivers' problems in a timely manner and provide constructive suggestions^[26]. Relevant studies have shown that guide-based symptom cluster management can effectively control symptom deterioration and improve the quality of life of patients^[27]. Ma Wenqing et al. found that symptom management programs can improve symptom management awareness and health promotion knowledge of patients and caregivers, increase their compliance, and improve their self-efficacy and treatment efficiency^[28]. Therefore, making full use of the self-efficacy potential of the research subjects, providing caregivers with disease-related knowledge education and constructive suggestions in real time, and alleviating negative emotions can increase their self-efficacy.

3.2 The Focus intervention can reduce the burden among caregivers of patients with advanced lung cancer

The burden of care refers to the psychological and emotional difficulties experienced by family members during the process of disease development and care^[29]. The study showed that 45.92% of the primary caregivers had been providing care for more than 6 months, and long-term and lasting care work had negative effects on the physical, psychological and social life of the caregivers^[30].

This study showed that there was no statistically significant difference in the level of caregiver burden between the two groups at baseline ($P>0.05$). At the 4th week of the intervention, the burden of care in the test group (41.65 ± 2.735 points) was lower than that in the control group (47.33 ± 7.066 points), At the 8-week follow-up, the burden of care in the test group (37.04 ± 4.758) was lower than that in the control group (47.48 ± 8.056), All of them were statistically significant ($P < 0.05$). Thus, at 4 weeks of the intervention and at the 8-week follow-up, the burden of caregivers was significantly lower than at baseline; moreover, the rate of decrease was greater in the intervention group, and the burden increase in the control group between the 4-week intervention and the 8-week follow-up. It can be seen that there are different trends of change. Although there was a decrease in all patients, the decrease in the experimental group was greater than that in the control group, indicating that the FOCUS program can reduce the caregiver burden of the caregivers of advanced lung cancer patients.

Porter's research shows that to reduce the burden of caring for cancer patients, it is necessary not only to improve their care skills but also to improve their ability to cope with stress^[31]. Thus, the FOCUS program reduces the burden of care. This is consistent with the research results of Shin J Y, who examine how to improve caregivers' emotional support, improve their ability to cope with stress, and further reduce caregivers' caregiver burden^[32].

3.3The FOCUS program improved the coping style of caregivers of patients with advanced lung cancer

Coping styles, also known as coping strategies, refer to cognitive and behavioral responses to pressure, frustration and stressful events. The more active the coping style was, the more motivated the caregiving behavior was, and the lower the disease burden was^[33]. When enrolled in this study, the survey showed that the coping style scores of caregivers of advanced lung cancer patients in the two groups were 28.78 ± 3.780 points in the control group and 28.78 ± 7.000 points in the experimental group, both of which were not high and basically consistent with other studies^[34].

In this study, the effect of the FOCUS intervention on caregivers of patients with advanced cancer was verified by referring to relevant literature^[35]. The data showed that there was no statistically significant difference in coping styles between the two groups at baseline ($P>0.05$). At the 4th week of the intervention, the coping style of the test group (33.20 ± 5.533 points) was more positive than that of the control group (28.76 ± 3.420 points), After 8 weeks of follow-up, the coping style score of the study group (35.39 ± 6.221) was still more positive than that of the control group (27.57 ± 3.854), All of them were statistically significant ($P<0.05$). At the 4th week of the intervention and at the 8-week follow-up, coping style scores showed a decreasing trend in the test group, while the scores in the control group showed a slow downward trend. The FOCUS program had a positive effect on caregivers and can significantly improve the coping style of caregivers of patients with lung cancer late.

3.4 The Focus program can improve the state of mind of caregivers of patients with advanced lung cancer

A state of mind is a weak and persistent emotional or emotional arousal state that is contagious and caused by environmental stimuli^[36]. Relevant research has shown that psychological stress can cause

individuals to experience strong negative emotions^[37]. Therefore, cultivating an individual's positive state of mind and eliminating or reducing his or her negative state of mind are effective ways to improve individual mental health. The results of this study showed that there was no statistically significant difference in mood states between the two groups of caregivers at baseline ($P>0.05$). At the 4th week of the intervention and at the 8-week follow-up, mood state scores were significantly lower in the test group, while scores in the control group showed a slow downward trend, thus indicating that the caregivers' state of mind was better in the experimental group than in the control group. The FOCUS program was shown to have a positive effect on caregivers by improving their mood.

In this study, exercise was considered an objective and scientific means of nondrug intervention, as it has been shown to help restore a healthy life state. Cognitive restructuring can occur when caregivers participate in sports; they may experience pleasant feelings when they participate in movement, thus improving bad states of mind, alleviating negative emotions, improving positive emotions, and promoting individual mental health. These findings are consistent with results from other scholars^[38]. In the Focus intervention, caregivers are guided to actively participate, and the subjective positive mood state of caregivers is promoted.

3.5 Limitations

Due to limitations regarding caregivers' age, their close relationship with patients and other conditions, this study used a quasi-experimental design rather than a randomized controlled trial; therefore, the results may be biased to a certain extent. Due to the limited course of diseases in superior hospitals and the limited time and energy of researchers, participants were only recruited from one hospital, and thus, the representativeness of the sample needs to be improved.

Conclusion

The FOCUS program can effectively improve caregivers' general self-efficacy, reduce caregivers' burden, improve caregivers' coping styles and improve caregivers' state of mind. This program can be extended to caregivers of patients with other terminal diseases and can be used to provide a sufficient basis for cancer care and hospice care.

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Authors have no conflict of interest to declare

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The data that support the findings of this study are available from the corresponding author upon reasonable request

Code availability: (software application or custom code) :

N/A Not applicable

Authors' contributions: (include appropriate statements)

Qinxue Zhou : Writing - Original Draft preparation; **Lihua Huang** : Conceptualization, Methodology, Writing - Review & Editing

Su Yang: Data curation; **Hui Han** : Project administration; **Lijuan Shen** : Supervision; **Jianli Cai** : Investigation.

MeiYuan Xing Literature Search

Ethics approval: (include appropriate approvals or waivers)

The project obtained ethical approval from The First Affiliated Hospital, Zhejiang University School of Medicine and The First People's Hospital of Huzhou

Consent to participate: (include appropriate statements)

Consent was obtained from the study subjects and informed consent was signed for this study

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