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Meta-analysis of the incidence and influencing factors of frailty in elderly stroke patients in China

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Abstract: *This study aimed to systematically evaluate the status and influencing factors of frailty in elderly stroke patients in China. Methods Literature about the incidence and influencing factors of frailty in elderly stroke patients in China were retrieved from CNKI, Wanfang database, VIP, CBM, PubMed, Embase, Web of Science and Cochrane Library. The retrieval time was from the establishment of the database to June 2024. Meta-analysis was performed using RevMan5.3 and Stata 14.0 software. Results A total of 20 articles were included. The results of Meta-analysis showed that the incidence of frailty in elderly stroke patients in China was 49.0 % [95 % CI (38.0 % -60.0 %)]. Among them, age, malnutrition, multi-disease coexistence, depression, sleep disorders, impaired activities of daily living, severe neurological impairment, multiple medication, history of falls, and living alone were risk factors; physical exercise is a protective factor. Conclusion The incidence of frailty in elderly stroke patients in China is high, and there are many risk factors. Medical staff should pay attention to the early screening and identification of risk factors in elderly stroke patients to reduce the occurrence of frailty.*

Keywords: *stroke; frailty; old age; incidence rate; influencing factors; meta-analysis*

1. Introduction

Stroke is an acute focal injury of the central nervous system of vascular causes. It is the first cause of death and disability in adults in China [1-2]. It is reported that elderly stroke patients over 60 years old in China account for 48.49 % [3]. Frailty is a clinical syndrome of decreased physical reserve and multiple system disorders, which reduces the body 's ability to cope with stress and maintain balance, and increases vulnerability to acute stressors[4] . Due to the decrease of physiological reserve capacity, psychological stress ability and social function, elderly stroke patients can produce different degrees of frailty[5], resulting in a significant increase in disability rate, mortality rate, complication rate and readmission rate[6]. Therefore, it is of great significance to understand the current situation and influencing factors of frailty in elderly stroke patients, which is conducive to improving their attention to frailty and promoting health management. Some scholars have carried out research on the influencing factors of frailty in elderly stroke, but due to the limitation of sample size, research area and other factors, there is a big difference between the results of each study. Therefore, this study used meta-analysis to explore the incidence and influencing factors of frailty in elderly stroke patients in China, in order to provide a theoretical reference for clinical medical staff in early identification and intervention. This study has been registered in PROSPERO (registration number : CRD-42024572692).

2. Data and Methods

2.1 Literature inclusion and exclusion criteria

2.1.1 Inclusion criteria

(1) The subjects were Chinese people aged ≥ 60 years old, who were definitely diagnosed as stroke. (2) Cross-sectional study, case-control study and cohort study ; (3) There were clear frailty measurement methods or survey tools in the study ; (4) The outcome indicators were the incidence and risk factors of frailty in elderly stroke patients.

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2.1.2 Excluded criteria

(1) unable to obtain the full text, data incomplete literature ;(2) non-Chinese and English literature ; (3) literature with low quality evaluation ;(4) Conference papers, reviews, case reports, etc.

2.2 Literature source and retrieval strategy

A total of eight Chinese and English databases (China National Knowledge Infrastructure, Wanfang Database, Weipu Network, China Biomedical Literature Database, PubMed, Embase, Web of Science, Cochrane Library) were searched by computer to collect studies on the incidence and influencing factors of frailty in elderly stroke patients in China published from the establishment of the database to June 2024. The Chinese search terms were ' elderly / elderly / elderly ', ' stroke / stroke / cerebrovascular accident / cerebral hemorrhage / cerebral ischemia / cerebral infarction ', ' frailty / frailty syndrome / frailty ', ' influencing factors / related factors / risk factors / risk factors '. English search terms were ' older / elderly / aged ', ' stroke / cerebrovascular accident / cerebral infarction / cerebral embolism / cerebral hemorrhage ', ' frail / frailty / frailty syndrome / asthenia / debility / debilities / weakness ', ' Risk Factors * / relevant factors * / influence factors / associated factors '.

2.3 Literature screening and data extraction

Two researchers independently screened the retrieved literature according to the inclusion and exclusion criteria. If there are differences, a third researcher will be invited to participate in the discussion and jointly determine the final inclusion of the literature. Data extraction included the first author, year of publication, research area, research type, sample size, number of frailty, incidence of frailty, frailty assessment tools, and influencing factors. (If two or more studies mentioned the same influencing factor, the factor was included).

2.4 Literature quality evaluation

The Newcastle-Ottawa scale (NOS)[7] was used to evaluate the quality of the case-control study and cohort study. It contains 8 items, with a total score of 9 points, and > 6 points are considered to be high-quality literature. Cross-sectional studies were evaluated using the cross-sectional study evaluation criteria recommended by the Agency for Healthcare Research and Quality (AHRQ) [8]. It contains 11 items with a total score of 11 points. According to the score from high to low, it is divided into high-quality research (8 ~ 11 points), medium-quality research (4 ~ 7 points), and low-quality research (0 ~ 3 points).

2.5 Statistically treated

Meta-analysis was performed using RevMan5.3 and Stata 14.0 software. The enumeration data were described by OR value and 95 % CI. The heterogeneity was evaluated by Q test and I^2 test. If there was no statistical heterogeneity among the studies ($I^2 \leq 50$ % and $P > 0.1$), the fixed effect model was selected for meta-analysis. Otherwise, the random effect model was selected for meta-analysis, and the source of heterogeneity was explored by subgroup analysis and sensitivity analysis. The methods of sensitivity analysis include eliminating the literature one by one and replacing the effect model. Egger 's test was used to determine whether there was publication bias in the literature with the incidence of reports and the number of any risk factors ≥ 10. $P < 0.05$ was considered statistically significant.

3. Results

3.1 Literature screening process and results

A total of 1013 articles were obtained by preliminary search. After layer-by-layer screening, 19 articles were finally included[9-28]. The screening process and results of the literature are shown in Figure.1.

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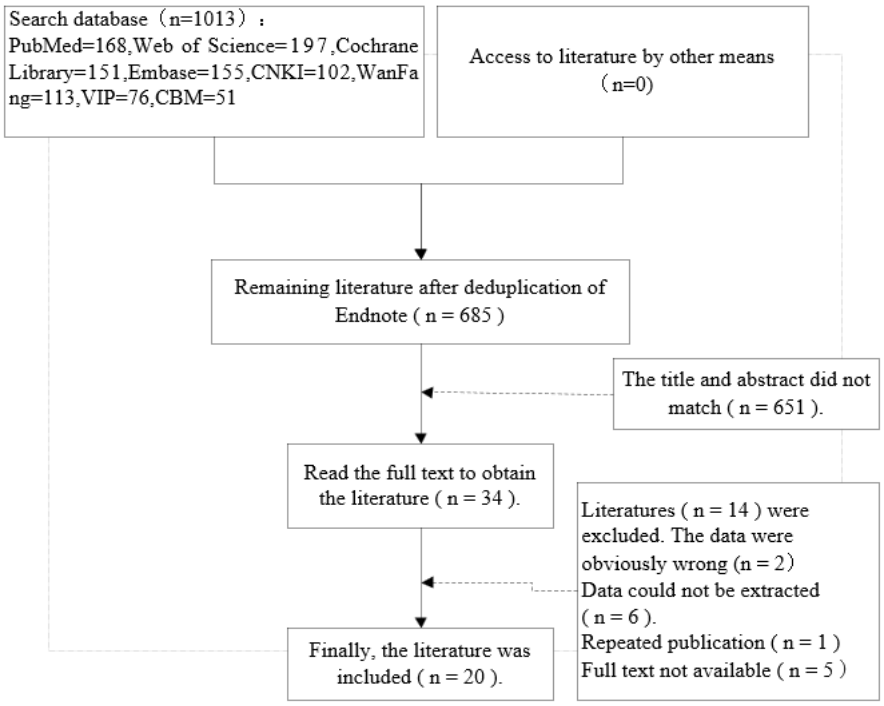

Figure 1 Literature screening process and results

3.2 The basic characteristics and quality evaluation results of the included literature

A total of 5250 elderly stroke patients were included in the 20 articles[9-28]. The quality evaluation of all literatures was medium and high quality. The basic characteristics and quality evaluation results of the included literature are shown in Table 1.

Table 1: The basic characteristics and quality evaluation results of the included literature

Included studies	Study location	research type	sample size (n)	Frailty number of people (n)	Incidence frailty (%)	offrailty assessment tools	Impact Factors	Literature quality score (points)
Fan fan2018[9]	Chengdu	case-control study	217	56	25.8	(1)	A	7a
Shangxiaofeng2020[10]	Shangqiu	case-control study	118	33	27.9	(1)	AG	6a
Zhao Jiaqi2020[11]	Liaoning	cross section study	242	180	74.4	(3)	AB	7b
Lin Wei 2021[12]	Guangxi	cohort study	124	78	62.9	(1)	CEFH	6a
Xia Hanyue2022[13]	Changsha	cross section study	328	272	82.9	(3)	BS	6b
Liu Lingling2022[14]	Changsha	cross section study	505	439	86.9	(3)	ADE	7b
Wang Lingyu2022[15]	Beijing	cross section study	98	15	15.3	(5)	AI	7b
Dou Li 2023[16]	Xinjiang	cross section study	223	27	12.11	(1)	ABE	5b
Zhang Xinyu 2023[17]	Liaoning	cross section study	532	249	46.8	(4)	ADFIKL	7b
Gao Xiao2023[18]	Jinan	cross section study	331	196	59.2	(1)	CHMNS	7b
Huangjiaojiao2023[19]	Shangqiu	case-control study	112	53	47.32	(4)	BDFL	7b
Qiao Huijuan2023[20]	Shangqiu	cross section study	94	59	62.77	(3)	BCEFGH	7b
Huang Yanan 2023[21]	Lanzhou	cross section study	618	331	53.6	(3)	ACEHJ	8b
Zhao Yidi2023[22]	Hunan	cross section study	240	146	71.6	(3)	OT	6b
Qian Junhong2023[23]	Zhengzhou	cross section study	250	75	30.14	(3)	BFKL	8b
ChenZhangjing2023[24]	Ningbo	cohort study	156	57	36.53	(2)	AP	6a
Wang Ruijuan2024[25]	Zhejiang	cohort study	146	41	28.05	(1)	AEGJ	6a
Jiang Xiaoling2024[26]	Bengbu	case-control study	231	109	47.18	(1)	CGHIK	6a
Zhang Linghui2024[27]	Qingdao	cohort study	485	134	25.57	(3)	EGMO	7a
Wang Genqun2024[28]	Shenzhen	Cross section study	200	172	86	(3)	DEO	7b

Note : 1 The ' FRAIL ' Scale ; 2 Fried 's Frailty Phenotype ; (3) Tilburg Frailty Indicator (TFI) ; 4 elderly frailty assessment scale (EFAS) ; 5 Frailty Index (FI) ;
A : age ; B : Combined disease ; C : multiple drug use ; D : impaired activities of daily living ; E : depression ; F : sleep disorders ; G : neurological impairment ; H : malnutrition ; I : Fall history ; J : Cognitive impairment ; K : living alone ; L : Physical exercise ; M : stroke frequency ; N : Educational level ; O : Social support ; P : Dysphagia ; Q: Degree of disability ; R : limb motor dysfunction ; S: Self-perceived burden ; a Using NOS score ; b AHRQ score ;

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3.3 Meta-analysis results

3.3.1 Meta-analysis of frailty in elderly stroke patients in China

The included 20 articles [9-28] reported the incidence of frailty in elderly stroke patients in China, and there was statistical heterogeneity among the literatures ($I^2 = 98.45$ %, $P < 0.05$). Meta-analysis was performed using a random effect model. The results showed that the incidence of frailty in elderly stroke patients in China was 49 % [95 % CI (38 %, 60 %)], as shown in Figure 2. Subgroup analysis was performed using the study area, frailty assessment tools, and study type, as shown in Table 2.

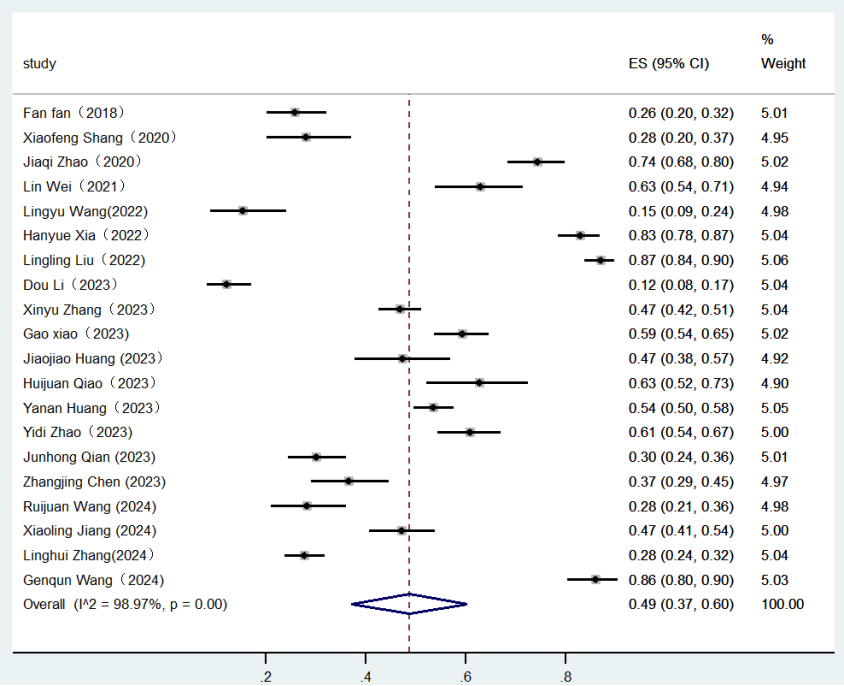

Figure 2 Forest map of the incidence of frailty among elderly residents in Chinese communities

Table 2 Subgroup analysis results of the incidence of frailty among elderly stroke patients in China

Subgroup	study number	frailty incidence (95%CI)	I^2*value*	*P*value
frailty assessment tools				
frail scale	7[9-10,12,16,18,25-26,]	37%(22%,52%)	97.14%	<0.001
Tilburg frailty indicator	10[11,13-14,20-23,27]	52%(39%, 65%)	98.85%	<0.001
problem area				
Central China region	7[10,13-14,19-20,22-23]	58%(38%, 77%)	98.52%	<0.001
East China region	5[18,22,24-25,27]	40%(27%, 53%)	95.89%	<0.001
Northeast China	2[11-17]	56%(52%, 59%)	—	—
Northwest region	2[16,21]	41%(38%, 45%)	—	—
Gender				
Female	14	45%(34%, 56%)	93.21%	<0.001
Male	14	41%(31%, 50%)	93.77%	<0.001

3.3.2 Influencing factors of stroke frailty in Chinese elderly

The results of Meta-analysis showed that age, chronic diseases, impaired activities of daily living, depression, sleep disorders, severe neurological impairment, multiple medications ≥3, malnutrition, history of falls, cognitive impairment, living alone, and physical exercise were the influencing factors of frailty in elderly stroke patients in China ($P < 0.05$), as shown in table 3.

Table 3 Meta-analysis results of influencing factors of frailty in elderly stroke patients in China

Influencing factors	The included literature(article)	Heterogeneity test		effect model	OR(95%CI)	*Z* value	*P* value
		I^2(%)	*P* value				
Age	9[9-11,14-17,21,24,25]	86%		<0.001	Random effect model	1.12[1.06,1.17]	4.28
Combined chronic diseases	5[13,16,19,20,23]	99%		<0.001	Random effect model	2.72[1.23,6.05]	2.46
Depression	7[12,14,16,20-21,15,27]	93%		<0.001	Random effect model	2.64[1.76,3.98]	4.66
Sleep disorders	5[12,17,19,20,23]	97%		<0.001	Random effect model	2.94[1.80,4.80]	4.31
Impaired activities of daily living	3[14,17,19]	83%		0.003	Random effect model	2.59[1.34,5.00]	2.83
Neurological impairment is severe	5[16,20,25-27]	88%		<0.001	Random effect model	3.25[1.65,6.39]	3.41
Multiple drug use ≥ 3 kinds	5[12,18,20,21,27]	88%		<0.001	Random effect model	3.63[1.24,10.61]	2.35

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Malnutrition	5[12,18,20-21,26]	93%	<0.001	Random effect model	4.05[1.30,12.66] 2.40
History of falls	3[15,17,26]	0%	0.46	Fixed effect model	4.61 [2.65, 8.00] 5.43
Cognitive impairment	2[21,25]	78%	0.001	Random effect model	5.11 [2.64, 9.88] 4.85
Living alone	3[17,23,26]	75%	0.02	Random effect model	2.70 [1.12, 6.51] 2.20
Physical exercise	2[17,19]	0%	0.67	Fixed effect model	0.33 [0.22, 0.50] 5.19

3.3.3 Sensitivity analysis and publication bias results

The sensitivity analysis was carried out after each study was eliminated in turn by one-by-one elimination method. The conclusion of the study did not change significantly, indicating that the stability of the Meta-analysis results was good, as shown in Figure 3. Through the conversion effect model, the Meta-analysis results of the influencing factors were compared and analyzed. It was found that the effect values were similar and the results were stable, as shown in table 4. Because the number of literatures included in each influencing factor was less than 10, no publication bias test was performed.

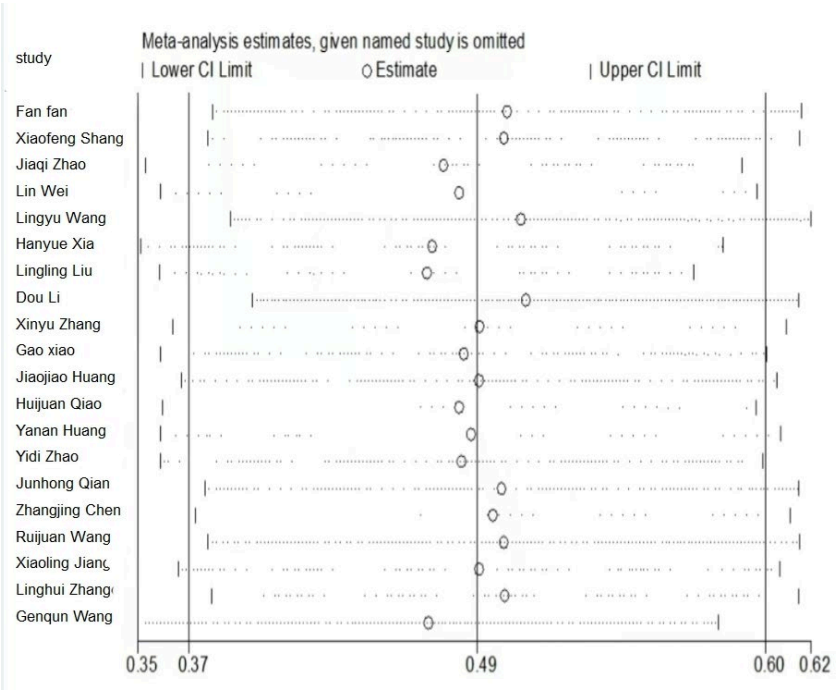

Figure 3: Sensitivity analysis of influencing factors of frailty in elderly stroke patients in China

Table 4 Sensitivity analysis results of influencing factors of frailty in elderly stroke patients in China

Influencing factors	Random effects model combined OR value (95 % CI)	P value	Fixed effect model combined OR value (95 % CI)	*P* value
Age	1.12 [1.06, 1.17]	<0.001	1.05 [1.03, 1.06]	<0.001
Combined chronic diseases	2.72 [1.23, 6.05]	<0.001	1.74 [1.66, 1.82]	<0.001
Depression	2.64 [1.76, 3.98]	<0.001	1.34 [1.27, 1.42]	<0.001
Sleep disorders	2.94 [1.80, 4.80]	<0.001	1.58 [1.49, 1.67]	<0.001
Impaired activities of daily living	2.59 [1.34, 5.00]	0.003	1.82 [1.69, 1.96]	<0.001
Neurological impairment is severe	3.25 [1.65, 6.39]	<0.001	3.12 [2.59, 3.77]	<0.001
Multiple drug use ≥ 3 kinds	3.63[1.24, 10.61]	<0.001	5.37 [3.94, 7.32]	<0.001
Malnutrition	4.05[1.30, 12.66]	<0.001	5.34 [4.02, 7.10]	<0.001
History of falls	4.61 [2.65, 8.00]	0.46	4.61 [2.65, 8.00]	<0.001
Cognitive impairment	5.11 [2.64, 9.88]	0.001	2.77 [1.81, 4.24]	<0.001
Living alone	2.70 [1.12, 6.51]	0.02	0.33 [0.22, 0.50]	<0.001

4. Discussion

The results of this study showed that the incidence of frailty in elderly stroke patients in China was 49 % [95 % CI (38 %, 60 %)], which was at a high level, lower than 66.8 % reported by foreign scholars such as Burton[29]in 2022. This may be related to sample size, regional differences, and differences in living environment.

The results of subgroup analysis showed that there were significant differences in the incidence of frailty in elderly stroke patients in China in terms of gender, region and assessment tools. Female patients

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have a higher incidence, mainly due to decreased estrogen levels after menopause, affecting bone mineral density and muscle strength, thereby increasing the risk of frailty [30]. The results of different assessment tools are significantly different. In this study, the detection rate of Tilburg frailty scale is higher than that of FRAIL scale. The reason is that FRAIL only evaluates the physical dimension, while Tilburg scale comprehensively evaluates from three aspects of body, psychology and society, and the results are more comprehensive and accurate. In view of the fact that there is no unified diagnostic standard for frailty, it is recommended to flexibly select evaluation tools in combination with the actual situation of patients. Regionally, the incidence of frailty in Central China is higher than that in South China and Northwest China, which may be related to the differences in lifestyle and eating habits in different regions.

The results of this study show that age is a risk factor for frailty in elderly stroke patients. The older the age, the higher the risk of frailty, similar to foreign studies[31]. This may be because the elderly with age, the system function decline, anti-stress ability decline, and thus the lack of effective resistance to adverse external stimuli, resulting in increased incidence of frailty[32]. In addition, elderly stroke patients are often accompanied by sequelae such as hemiplegia, swallowing or speech disorders, and decreased activities of daily living, which will increase the risk of frailty to a certain extent. Therefore, clinical medical staff should pay attention to elderly stroke patients, regularly evaluate their frailty, and formulate frailty intervention management programs for stroke patients of different ages to delay the frailty caused by age as much as possible.

The results show that patients with impaired activities of daily living have a higher risk of frailty, which is similar to the results reported by Song Yingying et al.[33]. With the increase of age, the functions of the elderly 's body decline, and different degrees of language, movement and cognitive impairment occur, which leads to the decline of activities of daily living and induces weakness. At the same time, some patients with severe stroke are accompanied by limb dysfunction. Patients need to take care of washing, activities, transfer and other aspects. At the same time, the limitation of the scope of activities will lead to negative emotions, physical and mental frustration and frailty. Therefore, during the hospitalization of elderly stroke patients, medical staff should arrange appropriate rehabilitation training to help patients recover their daily living ability and minimize their dependence on others, thereby reducing the risk of frailty.

Previous studies have confirmed that the history of falls is a risk factor for frailty in elderly stroke patients[34], and the results of this study are consistent with it. Elderly stroke patients have many problems such as multi-system dysfunction, decreased balance ability, decreased stress and resistance, which can further promote the occurrence and progress of frailty. This study also shows that physical exercise is a protective factor for frailty in elderly stroke patients. According to the relevant guidelines,[35] the elderly over 65 years old should complete at least 150 minutes of moderate-intensity aerobic exercise per week, which can effectively improve the central nervous and immune function, improve the activity ability, delay the progression of sarcopenia and reduce the risk of falls. Therefore, medical staff should formulate individualized and step-by-step exercise programs based on the age and physical function of patients, which is of great clinical significance for enhancing immunity, improving health status and delaying the process of frailty.

Studies have shown that[36], the presence of sleep disorders will not only affect the mental state, but also endanger the health and increase the risk of weakness, the results of this study are consistent with this. At the same time, studies have shown that the incidence of sleep disorders is higher in frail elderly people, and sleep disorders can effectively predict the outcome of frailty[37]. Therefore, medical staff should pay attention to the sleep quality of the elderly. Good sleep quality is conducive to the recovery of neurological function after stroke and the maintenance of normal cognition, so as to carry out daily life. If the sleep quality of patients is poor, traditional Chinese medicine treatment or drug intervention should be given to patients if necessary.

Relevant epidemiological data show that the incidence of multi-disease coexistence in elderly stroke patients is 43 % ~ 99 %[38]. When combined with three or more chronic diseases, the body is in a state of chronic consumption for a long time, which not only accelerates the degradation of multiple organ functions, but also superimposes stroke sequelae, significantly increasing the difficulty of disease management and the risk of frailty. The coexistence of multiple diseases is often accompanied by multiple medications. This study confirms that multiple medications are risk factors for frailty in elderly stroke patients in China. The organ function of the elderly decreases with age. Polypharmacy can easily lead to drug interactions, adverse reactions and irrational drug use, which further increases the risk of frailty. Therefore, it is necessary to closely monitor the coexistence of multiple diseases and the progression of frailty in patients. Medical institutions need to strengthen the risk management training of elderly medication for medical staff, identify the adverse effects of drugs in the early stage, and standardize and

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streamline prescriptions on the premise of ensuring efficacy.

Similar to the results of Qi et al.[39], the worse the nutritional status in this study, the higher the incidence of frailty. With the increase of age, the oral function of stroke patients decreases, and the possibility of poor appetite, difficulty in eating and difficulty in swallowing is greater, which leads to insufficient long-term nutritional intake of the body. The demand for nutrients such as energy and protein cannot meet the needs of the body, and the muscle content decreases, aggravating the degree of weakness [40]. Therefore, medical staff should carry out screening for frailty and malnutrition in elderly stroke patients, and carry out targeted dietary guidance for patients at risk of malnutrition according to the screening results, and strengthen nutritional health education to improve the nutritional status of patients and reduce the occurrence of malnutrition.

Many studies have confirmed that depression is closely related to the occurrence and development of frailty [41-42]. The incidence of depression in elderly stroke patients with frailty is high, which is mainly related to the acute stress response caused by changes in the hospital environment, sudden limb and speech disorders. At the same time, patients are prone to significant psychological burden and further increase the risk of depression in the face of multiple pressures such as disease treatment, medical expenses, potential sequelae and family care support. Depression is often manifested as low mood and social withdrawal, which will reduce treatment compliance and acceptance of health education, form a vicious circle, and accelerate the progress of weakness. Therefore, medical staff and family members should focus on the mental health of patients, and timely carry out psychological assessment and intervention guidance. Patients are encouraged to participate in social and cultural activities such as choirs, ballroom dancing, and tai chi, so as to alleviate negative emotions and block the interaction between depression and frailty.

This study also found that severe neurological deficit is a risk factor for frailty in elderly stroke patients. NIHSS score can comprehensively evaluate the degree of nerve defect in patients, including consciousness, instruction, visual field, language, limb and so on. The higher the NHISS score, the more severe the nerve injury, which may be accompanied by other functional injuries, such as limb motor dysfunction, speech disorder and dysphagia, thereby increasing the risk of frailty. Therefore, medical staff need to evaluate the neurological impairment of elderly stroke patients in a timely manner and choose appropriate rehabilitation methods for treatment ; for patients with higher NHISS scores, attention should be paid to disease management and health education, and more support should be provided as much as possible.

There are some limitations in this study : (1) The research included in this study is mainly a cross-sectional study. Compared with prospective studies, its demonstration is weak and vulnerable to the interference of confounding factors, resulting in bias in the research results. (2) There are obvious differences in the combination of some influencing factors in this study, and there are great differences between the frailty assessment tools used in each study, which may lead to bias in the incidence of frailty, influencing factors and the conclusions of this study. (3) Because some risk factors involve too few literatures, they are not combined, which may bias the research results. It is suggested that more large-sample, high-quality original studies and longitudinal studies should be carried out in the future to verify the stability of the results.

The results of comprehensive analysis showed that the incidence of frailty in elderly stroke patients in China was 49 %, and multiple potential risk factors were involved. Clinical medical staff should pay attention to the early assessment and accurate identification of frailty risk in this population, focus on high-risk groups such as advanced age, decreased daily living ability and coexistence of multiple diseases, and implement targeted intervention strategies. At the same time, it is necessary to strengthen the health education of frailty prevention and standardized management in elderly stroke patients, actively block the progress of risk factors, reduce the risk of frailty, and improve the physical function and overall quality of life of patients.

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