A Meta-analysis of the Incidence of Frailty and its Influencing Factors in Middle-aged and Elderly Inpatients with Hypertension

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Abstract: Objective: To systematically review the current status of frailty and its influencing factors in middle-aged and-elderly patients hospitalized with hypertension. Methods: Literature of CNKI, China Science and Technology Journal Database, Wanfang, PubMed, Embase, Medline, Web of Science and Cochrane Library on the factors affecting combined frailty in middle-aged and elderly hypertensive patients were searched to build the database until December 31, 2023, and Meta-analysis was conducted using RevMan5.4 software. Results: A total of 14 articles including 4097 middle-aged and elderly hypertensive patients were included. The Meta-analysis results showed that: The incidence of frailty in the middle-aged and elderly hypertensive patients was 36%. And A total of 13 contributing factors were statistically significant (P<0.05). Conclusion: The occurrence of frailty in middle-aged and elderly hypertensive hospitalized patients is affected by many factors. Medical staff should focus on the evaluation and management of high-risk groups, and make early intervention to reduce the occurrence of frailty and slow down the process of frailty.

***Keywords*:** hypertension, frailty, influencing factor, meta-analysis

1. Introduction

Hypertension is a chronic cardiovascular disease characterized by persistently high blood pressure, which is one of the most common chronic diseases[1]. With the improvement of living standards and the increase of work pressure, the trend of young age for hypertension patients is becoming more and more obvious[2]. Furthermore, studies have indicated that the prevalence of hypertension among middle-aged individuals aged 45 and above in China reaches as high as 41.74%[3]. Frailty is a biological syndrome characterized by the gradual degeneration of multiple physiological systems, leading to reduced bodily reserves, decreased resistance to stressors, and an increased likelihood of adverse outcomes[4]. Studies have shown that hypertension is positively correlated with the occurrence of frailty, with hypertensive patients having a 77% increased risk of developing frailty compared to the general population[5]. It is reported that the detection rate of frailty among hypertensive patients in China ranges from 13.8% to 53%[6-9]. A meta-analysis has shown that hypertensive patients with frailty have higher risks of death, hospitalization, and falls compared to non-frail hypertensive patients. Early reversal of the frailty process can significantly improve the quality of life for hypertensive patients, substantially reduce medical costs, and alleviate the financial burden on the country[10]. Therefore, based on evidence-based methods, this study extracted and analyzed the incidence and influencing factors of frailty in hypertensive patients, providing a basis for clinical healthcare providers to manage and intervene in at-risk populations.

2. Information and methods

2.1 Inclusion and exclusion criteria of the literature

Inclusion criteria:

The target population consists of hospitalized patients with a clearly defined diagnosis of hypertension, aged 40 years or older. The literature reviewed includes cross-sectional studies, case-control studies, retrospective studies, and cohort studies. The focus is on the influencing factors or risk factors associated with frailty in middle-aged and elderly hospitalized patients with hypertension. The included literature must have a clear definition of frailty and mention the method or survey tool used to assess frailty. The literature reviewed must have employed multivariate regression analysis, and the original data must provide OR/HR values or data that can be converted to such values.

Exclusion criteria:

Duplicate publications.Incomplete information or data that cannot be converted. Low-quality literature: Such as those scoring less than 5 on the Newcastle-Ottawa Scale or less than or equal to 3 on the bias risk assessment criteria recommended

by the Agency for Healthcare Research and Quality. Literature types: Reviews, case reports, or conference abstracts. Non-English or non-Chinese literature.

2.2 Search strategy

Computer search of CNKI, VIP, Wanfang, PubMed, Embase, Medline, Web of Science, Cochrane Library databases at home and abroad, the search time is for database construction to December 31,2023.

The search terms in Chinese and English are:Middle-aged and elderly / Adult / Middle aged / middle age / aged / older / elderly; Hypertension / high blood pressure /high blood pressures / blood pressure, high / blood pressures,high; Inpatients / hospitalization / patients; Frailty / frailty syndrome / frailties/ frailness /debility / debilities /Debilitation syndrome; influencing factors / risk factors / related factors / predictors /causes.

2.3 Literature screening and data extraction

Two researchers screened literature based on inclusion/exclusion criteria and extracted relevant data. Disagreements were resolved by a third researcher. Extracted information included general literature details (author/year/region/study type), study content (source of study subjects/sample size/assessment method for frailty), and outcome measures (number of frail individuals/influencing factors).

2.4 Literature quality evaluation

Evaluation of literature quality was performed by 2 investigators using the risk of literature bias assessment tool.Using the Newcastle-Ottawa Scale (NOS), cohort and case-control studies were rated for quality, with scores ranging from 0 to 9. Studies were classified as low (0-4), moderate (5-7), or high (>7) quality [11]. Cross-sectional studies were assessed using criteria recommended by the Agency for Healthcare Research and Quality (AHRQ), with scores from 0 to 11: low (0-3), moderate (4-7), and high (8-11) quality[12]. Quality assessments were independently conducted and cross-checked by two researchers, with disagreements resolved through discussion or consultation with a third researcher.

2.5 Statistical methods

Meta-analysis was conducted using RevMan5.4. For dichotomous data, odds ratio (OR) was used as the effect measure; for continuous data, mean difference (MD) was used. If $P>0.1$ and $I^2<50\%$, indicating acceptable heterogeneity, a fixed-effects model was used for pooling. If $P\leq0.1$ or $I^2\geq50\%$, suggesting substantial heterogeneity, a random-effects model was chosen. Statistical significance was set at $P<0.05$. Both fixed- and random-effects models were used to analyze pooled results, and sensitivity analysis was performed by comparing their differences.

3. Results

3.1 Retrieval results of literature

By searching relevant databases at home and abroad, 1746 articles were obtained, and the remaining 1239 duplicates were deleted. After reading the titles, abstracts and full texts, 14 articles were finally included.

3.2 Basic information of the included literature and quality evaluation results of the included literature

The 14 included studies were all cross-sectional, with 2 in English and 12 in Chinese. Two studies scored 8, indicating high quality. Seven scored 7, three scored 6, and two scored 5, totaling 12 studies of moderate quality. Basic characteristics of the included studies are shown in Table 1.

Table 1. Basic information on the inclusion of literature

Included in the study	Country	Frailty assessment tools	The type of research	Sample capacity	Frailty incidence	Frailty influencing factors	Literature quality score
Can Zhao 2023[13]	China	①	CSS	200	43.50%	3/5/7/8/15/24/25	6
Yixin Yan 2023[14]	China	①	CSS	360	39.7%	1/7/8/10/12	7
Xiuping Xu 2021[15]	China	③	CSS	450	20.44%	1/3/5/6/8/9/11/15 /16/18/22/23/26	5
Dan Xiao 2022[16]	China	①	CSS	380	31.57%	1/11/21/22	7

Included in the study	Country	Frailty assessment tools	The type of research	Sample capacity	Frailty incidence	Frailty influencing factors	Literature quality score
Xiao-jie wang 2021[17]	China	③	CSS	167	34.73%	1/4/13/14/15/16/17/18/19/27	7
Sijie Qiu 2023[18]	China	①	CSS	200	32%	1/28	5
Kunjie Liu 2022[9]	China	③	CSS	300	53%	1/3/4/5/6/9/17	7
Jin-fang Li 2018[19]	China	⑤	CSS	294	27.6%	1/2/11/16/23	7
Li Fan 2015[20]	China	④	CSS	320	23.1%	1/18/19/20/21	8
Ling Du 2022[21]	China	①	CSS	308	37.01%	3/13/14/20	7
Yan Cheng 2018[22]	China	③	CSS	153	30.7%	1/3/4/16/17/18	6
Li-li Chen 2020[23]	China	①	CSS	420	39.29%	1/8/10/11/12	8
Zhu, Y.2020[24]	China	②	CSS	242	25.6%	29/30/31	7
Sakyi, S.A.2023[25]	Republic of Ghana	⑥	CSS	303	59.7%	1/2/9/17/23	6

Notes: CSS: cross-sectional study; ① Fried Frailty Phenotype Scale; ② Frailty Index (FI); ③ Frailty Screening Scale (FRAIL); ④ 4 mGait pace assessment method; ⑤ Clinical Frailty Scale (CFS); ⑥ TFI Frailty Scale; 1. Age; 2. Sex; 3. Abnormal BMI value; 4. Systolic blood pressure level; 5. Smoking; 6. Drinking alcohol; 7. Sleep quality; 8. Cognitive dysfunction; 9. Education level; 10. And osteoporosis; 11. Risk of malnutrition; 12. MNA- -SF score; 13. Serum albumin value; 14. Hemoglobin value; 15. Dyslipidemia; 16. Multiple drugs; 17. Combined with diabetes mellitus; 18. Combined with coronary heart disease; 19. Combined with cerebrovascular disease; 20. Combined with chronic kidney disease; 21. Number of comorbidities; 22. Course of hypertension; 23. Comorbidity; 24. Combined with depression; 25. Combined with hyperglycemia;26. Hypertension grade; 27. combined chronic obstructive pulmonary disease; 28. serum hypersensitivity C-reactive protein level; 29. mean actual variability of 24-hour systolic blood pressure;30. mean actual variability of daytime systolic pressure; 31. mean actual variability of nighttime systolic pressure

3.3 Results of a meta-analysis of frailty incidence

14 studies reported frailty incidence in hospitalized hypertensive patients, totaling 4,097 cases for Meta-analysis. Using a random-effects model, the frailty incidence was 36% [95% CI: (0.29, 0.42), P<0.05], with statistically significant pooled results (see Figure 1).

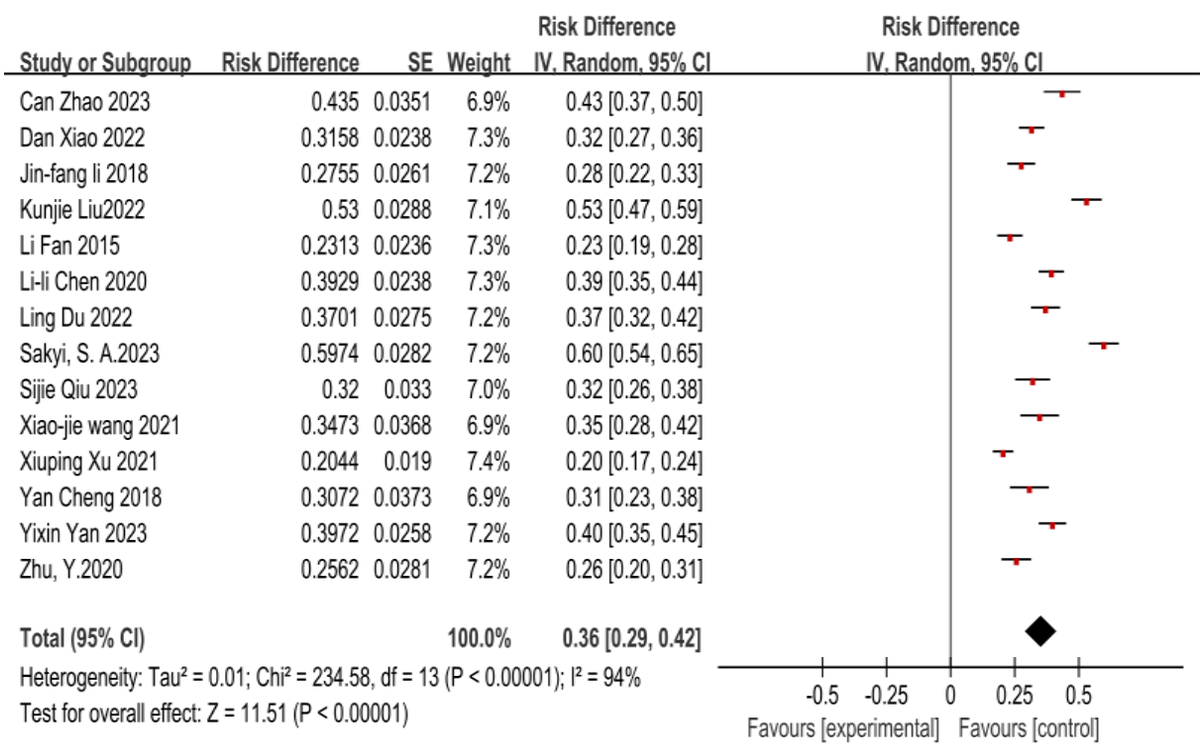

Figure 1. Results of a meta-analysis of frailty incidence

3.4 Results of meta-analysis of influencing factors

A Meta-analysis of 21 factors was conducted, with age and BMI categorized and analyzed separately as categorical and continuous variables. Results showed that 13 factors, including age, abnormal BMI, systolic blood pressure, osteoporosis, malnutrition risk, MNA-SF score, serum albumin, hemoglobin, dyslipidemia, polypharmacy, concurrent diabetes, coronary heart disease, and chronic kidney disease, were risk factors for frailty in middle-aged and elderly patients with hypertension (P<0.05). See Table 2.

Table 2. Results of Meta-analysis of influencing factors

influencing factors	Included literature	Heterogeneity test		Effect model	OR/SD	95% confidence interval	Z	P
		Q-test（P）	I^2（%）					
Age	8 3	< 0.05 < 0.05	99 86	random	MD=6.98 OR=7.06	3.72 ～ 10.24 2.13 ～ 23.39	4.20 3.2	< 0.05 < 0.05
Gender(Man)	2	0.03	78	random	OR=1.77	0.84 ～ 3.76	1.5	0.13
BMI unusual	3 2	0.02 < 0.05	73 98	random	OR=2.4 MD=-0.14	1.25 ～ 4.63 -4.32 ～ 4.03	2.62 0.07	< 0.05 0.95
Systolic blood pressure	3	0.01	77	random	MD=14.7	7.79 ～ 21.62	4.17	< 0.05
Smoke	3	0.02	75	random	OR=1.94	0.79 ～ 4.78	1.44	0.15
Drink	2	0.02	82	random	OR=2.07	0.77 ～ 5.54	1.44	0.15
Cognitive dysfunction	3	< 0.05	97	random	OR=1.44	0.17 ～ 12.28	0.33	0.74
High school and below	3	< 0.05	96	random	OR=2.39	0.38 ～ 14.83	0.93	0.35
Rarefaction of bone	2	0.59	0	fixed	OR=3.87	2.53 ～ 5.92	6.23	< 0.05
Malnutrition risk	4	< 0.05	94	random	OR=6.65	2.01 ～ 21.94	3.11	< 0.05
MNA-SF grade	2	0.19	42	fixed	MD=-2.76	-3.09 ～ -2.42	16.04	< 0.05
Serum albumin	2	< 0.05	89	random	MD=-6.31	-8.90 ～ -3.71	4.76	< 0.05
Hemoglobin	2	0.78	0	fixed	MD=-23.91	-25.93 ～ -21.89	23.19	< 0.05
Dyslipidemia	2	< 0.05	92	random	OR=7.15	1.26 ～ 40.59	2.22	0.03
Multiple medication	4	< 0.05	83	random	OR=5.89	2.48 ～ 13.97	4.02	< 0.05
Combined with diabetes	4	< 0.05	83	random	OR=3.41	1.65 ～ 7.03	3.31	< 0.05
Combined with coronary heart disease	4	< 0.05	82	random	OR=3.28	1.53 ～ 7.07	3.04	< 0.05
Combined with cerebrovascular disease	2	0.11	61	random	OR=1.87	0.95 ～ 3.69	1.82	0.07
With chronic kidney disease	2	< 0.05	85	random	OR=8.92	1.17 ～ 68.08	2.11	0.03
Number of comorbidities	2	< 0.05	99	random	MD=2.07	-0.61 ～ 4.74	1.52	0.13
Complication	2	< 0.05	87	random	OR=2.97	0.85 ～ 10.39	1.71	0.09

Notes: BMI: Body mass index; MNA-SF score: micro-nutrition score-brief table

3.5 Sensitivity analysis

Using random-effects and fixed-effects models to estimate ORs and 95% CIs, results showed directional changes in the effect model for BMI as a continuous variable, while other factors remained consistent, indicating stable study results. See Table 3.

Table 3. Results of the sensitivity analysis

Influencing Factors	Fixed			Random		
	OR/MD	95%CI	P	OR/MD	95%CI	P
Age Continuous	9.17	[8.85, 9.49]	< 0.05	6.98	[3.72, 10.24]	< 0.05
Classified	5.67	[3.82, 8.41]	< 0.05	7.06	[2.13, 23.39]	< 0.05
BMI Classified	2.13	[1.54, 2.93]	< 0.05	2.4	[1.25, 4.63]	< 0.05
Continuous	1.04	[0.51, 1.58]	< 0.05	-0.14	[-4.32, 4.03]	0.95
Systolic Blood Pressure	17.91	[15.48, 20.34]	< 0.05	14.7	[7.79, 21.62]	< 0.05
Rarefaction of Bone	3.87	[2.53, 5.92]	< 0.05	3.85	[2.52, 5.90]	< 0.05
Malnutrition Risk	5.88	[4.56, 7.59]	< 0.05	6.65	[2.01, 21.94]	< 0.05
MNA-SF Grade	-2.76	[-3.09, -2.42]	< 0.05	-2.76	[-3.20, -2.32]	< 0.05
Serum Albumin	-6.15	[-6.99, -5.31]	< 0.05	-6.31	[-8.90, -3.71]	< 0.05
Hemoglobin	-23.91	[-25.93, -21.89]	< 0.05	-23.91	[-25.93, -21.89]	< 0.05
Dyslipidemia	5.61	[3.72, 8.47]	< 0.05	7.15	[1.26, 40.59]	0.03
Multiple Medication	5.32	[3.81, 7.43]	< 0.05	5.89	[2.48, 13.97]	< 0.05
Combined with Diabetes	3.73	[2.81, 4.95]	< 0.05	3.41	[1.65, 7.03]	< 0.05
Combined with coronary Heart Disease	2.92	[2.15, 3.96]	< 0.05	3.28	[1.53, 7.07]	< 0.05
With Chronic Kidney Disease	6.45	[3.86, 10.78]	< 0.05	8.92	[1.17, 68.08]	0.03

3.6 Publication bias

A funnel plot of studies reporting frailty incidence showed that the effect sizes were roughly symmetrically distributed around the combined effect. However, due to the limited number of studies and high-quality literature included, publication bias could not be fully excluded (see Figure 2).

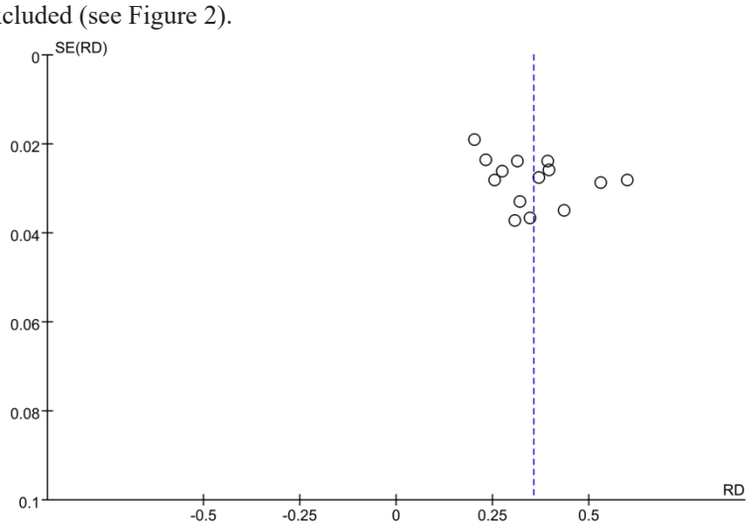

Figure 2. Funnel plot of frailty incidence in middle-and-elderly hypertensive inpatients

4. Conclusion

At present, the number of studies on weakness of hypertensive patients at home and abroad is increasing, indicating that weakness has been more and more widely valued. However, the incidence of frailty in hypertensive patients is still relatively high, indicating that frailty has not been well managed and intervened early. The results of meta-analysis in this study showed that the incidence of frailty in hypertensive patients was 36%.

Frailty in middle-aged and elderly inpatients with hypertension is influenced by various factors. Age: As age increases, the functional level of the body and organs of patients with hypertension gradually decline, and personal reserve capacity also decreases[26]. Systolic Blood Pressure: A study [27] found a U-shaped relationship between baseline systolic blood pressure (SBP) and frailty, indicating increased frailty risk at both low and high SBP levels. High SBP can cause vascular stiffening and plaque formation, reducing vessel elasticity, tissue perfusion, and oxygenation, thereby decreasing cerebral blood flow to motor areas and impairing physical function[28]. Low SBP may lead to frailty due to reduced blood flow and activity intolerance from inadequate blood supply.Frailty itself is characterized by the decline in the physiological ability of multiple organ systems[29]. At the same time, hypertension often causes a variety of cardiovascular and cerebrovascular diseases. Many diseases will lead to the abnormality of human multi-functional systems, and the abnormality of multiple systems will induce the occurrence of weakness more than that of a single system[30]. Nutritional status is a key regulator of frailty [31]. The mechanism of frailty caused by malnutrition may be due to malnutrition itself [32], which impairs normal muscle and immune system function, considered a crucial biological mechanism promoting frailty progression. And lower hemoglobin and albumin levels lead to a decrease in aerobic exercise capacity, decreased muscle strength, increased cognitive impairment and fatigue, increasing the risk of falls and disability, and promoting frailty[21].In summary, 13 factors including age, abnormal BMI, systolic blood pressure, osteoporosis, malnutrition risk, MNA-SF score, serum albumin, hemoglobin, dyslipidemia, polypharmacy, diabetes, coronary heart disease, and chronic kidney disease are risk factors for frailty in middle-aged and elderly patients with hypertension. Healthcare providers should prioritize assessment and management of high-risk groups, intervene early to reduce frailty incidence and slow its progression.

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