

Risk factors analysis of nosocomial pneumonia in elderly patients with acute cerebral infraction

Yang NanZhu, MD^a, Li Xin, PhD^{b,*}, Yun Xianghua, MD^c, Chen Jun, MD^d, Li Min, MD^d

Abstract

To investigate the risk factors of nosocomial pneumonia (NP) in elderly patients with acute cerebral infarction (ACI).

In this study, 324 aged 70 years and over patients with ACI who were admitted to the inpatient department of TianJin First Hospital (China) from January 2012 to February 2018 were retrospectively analyzed. The patients were divided into NP group (80 patients) and non-NP group (244 patients) according to whether NP was occurred 48 hours after hospitalization. Baseline profiles and biochemical analyses were compared between 2 groups. Information regarding risk factors for NP in elderly patients with ACI was collected from all patients. Associations with NP and outcome were evaluated.

Among the total patients, NP occurred in 80 (24.69%) patients. There were no statistically significant differences between risk of NP and sex, current drinking, diabetes mellitus, stroke history, and levels of serum UA, TG, HDL-C, LDL-C, Glucose, chloride, potassium. Multivariate logistic regression analysis showed that the independent risk factors for NP were living alone (OR 4.723; CI 1.743~12.802; $P=.002$), initial NIHSS score (OR 1.441; CI 1.191~1.743; $P=.000$), NRS2002 score (OR 0.139; CI 0.087~0.223; $P=.000$), BMI (OR 1.586; CI 1.353~1.858; $P=.000$), a past pneumonia history (OR 0.073; CI 0.017~0.321; $P=.001$), atrial fibrillation (AF) (OR 0.129; CI 0.033~0.499; $P=.003$), CRP (OR 1.050; CI 1.017~1.085; $P=.003$), BUN (OR 0.603; CI 0.448~0.812; $P=.001$) and Cr (OR 1.036; CI 1.015~1.057; $P=.001$). Level of albumin was an independent protective factor of NP in elderly patients with ACI (OR 0.865; CI 0.750~0.999; $P=.048$). Furthermore, elderly patients with ACI who had NP had worse clinical outcomes both during hospitalization and after discharge ($P<.05$).

We identified significant risk factors for NP in elderly patients with ACI, including living alone, initial NIHSS score, malnutrition, a past pneumonia history, AF, CRP, and Renal function were associated with NP in elderly patients with ACI. The clinical course was worse and the duration of hospital stay was longer in NP patients than in non-NP patients.

Abbreviations: ACI = acute cerebral infarction, AF = atrial fibrillation, ALB = albumin, BUN = blood urea nitrogen, CRP = C-reactive protein, FIB = fibrinogen, HAP = hospital-acquired pneumonia, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, ICU = intensive care unit, LDL-C = low-density lipoprotein cholesterol, NDS = neurological function deficit scale, NIHSS = National Institutes of Health Stroke Scale, NP = nosocomial pneumonia, NRS2002 = nutrition risk screening 2002, TC = total cholesterol, TG = triglycerides, TP = total protein, UA = uric acid, VAP = ventilator-associated pneumonia, WBC = serum white blood cell.

Keywords: acute cerebral infarction, National Institute of Health Stroke Scale, nosocomial pneumonia, nutritional status, risk factors

1. Introduction

Acute cerebral infarction (ACI) is the most common stroke type, accounting for 60% to 80% of all strokes. ACI occurs frequently in elderly people. Population aging has become a global concern in the past 2 decades.^[1] With the growth of the

aging population, incidence of cerebral infarction shows an increasing trend.^[2] Different gerontology experts defined further sub-groups of this population segment such as Forman et al^[3] who categorized generation 60 years and over in the “young old” (60–69 years), the “middle old” (70–79 years), and the “very old” (80+ y) persons. While our hospital is a secondary hospital, we have a Medical Comorbidity Ward and most of our patients were middle-aged and elderly people. In the elderly, alveolar bronchioles dilatation change, and respiratory muscle strength decline, resulting in decreased sputum expectoration ability and cough response in elderly patients, which is easy to be associated with nosocomial pneumonia (NP).

The term NP broadly covers all infections occurring 48 hours or more after hospital admission excluding any infection incubating at the time of admission. NP included hospital-acquired pneumonia (HAP), healthcare-associated pneumonia, and ventilator-associated pneumonia (VAP), which were defined according to the guidelines of the American Thoracic Society and Infectious Diseases Society of America.^[4] In this study, VAP were not included, because the patients who need endotracheal intubation and invasive mechanical ventilation were treated in intensive care unit (ICU).

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^a MD postgraduate of Neurology, ^b Department of Neurology, the Second Hospital of Tianjin Medical University, ^c Department of Neurology, ^d Department of Clinical laboratory, TianJin First Hospital, China.

* Correspondence: Li Xin, Department of Neurology, the Second Hospital of Tianjin Medical University, Tianjin 300211, China (e-mail: lixinsci@126.com).

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NP is one of the most common hospital-acquired infections, can be life-threatening, and often occurs in critically ill mechanically ventilated patients. It is one of the leading nosocomial infections worldwide which accounts for 13% to 18% of all nosocomial infections that affect 0.5% to 2.0% of hospitalized patients. In fact, HAP is as commonly found in Asian countries as in developed countries.^[5-7] NP is a growing concern because treatment options are limited and the mortality rate is high. The aim of this study was to assess the main risk factors of NP in elderly patients with ACI.

2. Material and methods

2.1. Study design

Patients with first-ever or recurrent acute ischemic stroke of any etiology admitted to the Stroke Unit of TianJin First Hospital (China) between January 2012 and February 2018 were consecutively screened. As a secondary comprehensive hospital in an important city of northern China, the vast majority of inpatients in our hospital are elderly. More than half of the hospitalized patients were older than 60, and nearly 30% of the hospitalized patients were older than 70. The hospital's medicine department treats approximately 3000 patients per year, with pulmonary, cardiovascular, gastro-intestinal, and nervous system diseases being the main disease groups for internal department. At our clinical centers, all patients who were clinically diagnosed with ischemic stroke were principally admitted and registered at the time of discharge, after providing informed consents. This study was approved by the Institutional Review Board at TianJin First Hospital. The consents obtained from all the participants were both informed and written.

2.2. Participants

The inclusion criteria were as follows: 70 years and over; an acute ischemic stroke; having CT or MRI scans on admission; neurological symptom onset within 3 days of hospital admission; and surviving more than 48 hours. NP is recognized if patients developed pneumonia at least 48 hours after hospitalization. Their clinical diagnosis was based on guidelines of the American Thoracic Society.^[4] The diagnostic criteria were: abnormal X-ray shadows in lungs and presence of at least 2 of the followings:

1. fever 38°C;
2. white blood cell abnormalities (increase or decrease);
3. purulent secretions.

Onset of clinical symptoms of pneumonia >48 hours after hospital-admission and sampling of respiratory secretion for microbiological diagnostics under the suspect of pneumonia

The exclusion criteria were as follows: Patients with intracranial hemorrhage, transient ischemic attack, severe multiple organ dysfunction, major trauma or surgery within half a year, signs and/or symptoms of infection within the 2 weeks before admission, reported use of antibiotics, having a history of cancer, hematologic disease, tuberculosis or immunosuppressants and corticosteroids during the 3 months prior to the stroke were excluded from the study.

2.3. Methods

We evaluated all the demographic data, including age, gender, clinical features, and pre-existing diseases. All biochemical

analyses were performed using routine methods at the local laboratory. Blood samples were taken from each patient routinely before treatment to measure serum white blood cell (WBC), C-reactive protein (CRP), D-dimer, total protein (TP), albumin (ALB), uric acid (UA), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glucose, electrolytes (sodium, chloride, and potassium), blood urea nitrogen (BUN), creatinine, fibrinogen (FIB) and homocysteine (Hcy). A physical examination, respiratory function test, posteroanterior chest X-ray, and electrocardiography performed before NP were evaluated, and complete blood counts were analyzed. Initial stroke severity was assessed daily from admission to discharge by well-trained neurologists using the National Institutes of Health Stroke Scale (NIHSS) score.

Nutrition Risk Screening 2002^[8] (NRS2002) was used to screen for nutritional risk, which was applied by a trained clinical examiner. NRS-2002 consists of 2 parts: the first is initial screening to be performed on all patients, devoted to the assessment of the patient's nutritional status and food intake problems, while the second contains information related to the impact of disease severity on nutritional status. Each part is scored from 0 to 3 points, and patients receive an extra point for age above 70 years. In total, the patient can get 7 points; the greater the number of points, the greater the risk of malnutrition. Patients with a total score of 3 or more (out of maximum score of 7) were considered to be at risk of malnutrition. In addition, all the patients involved were 70 years and over with an age score of 1 point. Body mass index was calculated as the patients' weight in kilograms divided by their squared height in meters.

The Neurological Function Deficit scale (NDS) evaluation is a rating tool for the comprehensive assessment of post-stroke functional disorders, involving level of consciousness, horizontal gaze, facial paralysis, speech, muscle strength of the upper limb, hand and lower limb, and walking ability. The NDS score is positively correlated with the degree of neurological deficits. The NDS score is divided into 6 grades: recovery, significant progress, progress, no change, deterioration and death. Three levels in front are valid, and the last 3 levels are invalid. The lower the NDS score, the better the clinical efficacy.

2.4. Statistical methods

Continuous variables with normal distribution were expressed as means±standard deviation. Categorical variables were expressed as numbers (percentages). Correlations between parametric variables were analyzed using Pearson correlation. Comparisons between independent groups for the values that were normally distributed were conducted using Student *t* test and between values not normally distributed using the Mann-Whitney *U* test. Variables with *P* < .05 from the results of the univariate analyses were considered confounders in the multivariable logistic regression analysis. A logistic regression analysis model was used to compare the correlation between independent variables and dependent variables. IBM SPSS Statistics, Version 22.0 software was used for all the above analyses. The level of significance was set at .05 (2-tailed).

3. Results

Ultimately, a total of 324 patients (male: n=162, 50%) were included in the analyses. The age ranged from 70 to 92 years (77.94±5.55). In the overall study subjects, 202 were 70 to

Table 1
Baseline characteristics of elderly patients with NP and non-NP with ACI.

	NP (n=80)	non-NP (n=244)	P
Males sex (%)	42 (52.50%)	120 (49.18%)	.606
Age (yr)	81.40±6.12	76.80±4.85	.000**
Current smoking (%)	25 (31.25%)	98 (40.16%)	.037*
Current drinking (%)	12 (15.00%)	40 (16.39%)	.768
Living alone (%)	42 (52.50%)	80 (32.79%)	.002**
Initial NIHSS score	6.28±5.04	2.19±2.12	.000**
NRS2002 score	5.86±0.94	3.93±1.01	.000**
Bed-ridden (%)	24 (30.00%)	10 (4.10%)	.000**
Body mass index (kg/m ²)	20.40±1.71	21.90±1.85	.019**
Hypertension (%)	54 (67.50%)	204 (83.61%)	.002**
Diabetes mellitus (%)	30 (37.5%)	98 (40.16%)	.673
Past pneumonia history (%)	30 (37.5%)	6 (2.46%)	.000**
AF (%)	14 (17.5%)	10 (4.10%)	.000**
Stroke history			
Cerebral infarction (%)	52 (65%)	138 (56.56%)	.183
Cerebral hemorrhage (%)	4 (5.0%)	6 (2.46%)	.254
WBC (×10 ⁹ /L)	7.80±2.93	6.34±1.98	.000**
CRP (mmol/L)	21.72±39.29	3.08±8.36	.000**
D-dimer (mmol/L)	0.28±0.35	0.17±0.85	.000**
TP (g/L)	62.24±11.37	65.28±8.63	.012*
ALB (g/L)	36.25±4.82	40.73±5.44	.000**
UA (mmol/L)	320±105.60	334.02±79.79	.219
TC (mmol/L)	4.47±1.10	5.29±4.64	.011*
TG (mmol/L)	2.89±9.51	2.62±9.28	.821
HDL-C (mmol/L)	1.21±0.35	1.30±0.49	.073
LDL-C (mmol/L)	2.64±1.02	2.92±1.43	.066
Glucose (mmol/L)	7.00±2.60	8.73±15.16	.088
Potassium (mmol/L)	3.86±0.64	3.86±0.38	.913
Sodium (mmol/L)	137.04±7.90	139.45±11.81	.036*
Chlorine (mmol/L)	102.46±6.09	104.39±2.71	.000**
Calcium (mmol/L)	2.21±0.79	2.25±0.90	.000**
BUN (mmol/L)	7.26±4.89	6.09±1.78	.002**
Creatinine (μmol/L)	85.50±60.44	75.29±20.55	.024*
Fibrinogen (mmol/L)	3.49±1.01	2.91±0.71	.000**
Homocysteine (mmol/L)	22.14±15.82	18.99±9.41	.032*

All data were expressed as mean ±SEM.

AF = atrial fibrillation, ACI = acute cerebral infarction, ALB = albumin, BMI = body mass index, BUN = blood urea nitrogen, CHOL = cholesterol, Cr = creatinine, CRP = C-reactive protein, HDL-C = high density lipoprotein-cholesterol, LDL-C = low density lipoprotein-cholesterol, NIHSS = National Institute of Health Stroke Scale, NRS2002 = nutritional risk screening 2002, TG = triglycerides, TP = total protein, UA = uric acid, WBC = white blood cell.

*P < .05.

**P < .01.

79 years old, 112 were 80 to 89 years old, and 10 were over 90 years old. Among them, 80 (24.69%) subjects developed NP 48 hours after hospitalization.

The baseline characteristics between groups with and without NP are presented in Table 1. The NP group presented with older age and higher rates of living alone, long-term bed condition, a past pneumonia history, atrial fibrillation (AF). They also had higher initial NIHSS score and NRS2002 score, levels of serum WBC, CRP, D-dimer, urea, creatinine, fibrinogen, homocysteine than that of the non-NP group ($P < .05$). At the same time, the NP group presented with lower rates of current smoking, hypertension, body mass index (BMI), and levels of serum ALB, TP, sodium, chlorine, calcium ($P < .05$). There were no statistically significant differences between risk of NP and sex, current drinking, diabetes mellitus, stroke history, and levels of serum Uric Acid UA, lipidemia (TG, HDL-C, LDL-C), Glucose, chloride, and potassium.

According to BMI, 59.57% (n=193) had BMI ≥ 20.5 kg/m². Among them, 68.85% (n=168) belonged to the non-NP group, and 31.25% (n=25) belonged to the NP group; A total of 122 patients (37.65%) had BMI range 18.5 kg/m² to 20.5 kg/m². Among them, 30.74% (n=75) belonged to the non-NP group, and 58.75% (n=47) belonged to the NP group; A total of 9 patients (2.78%) had BMI < 18.5 kg/m², which means undernourishment. Among them, 0.41% (n=1) belonged to the non-NP group, and 10% (n=8) belonged to the NP group; There was a significant difference between the NP group and non-NP group ($P = .019$).

According to NRS, 0.31% (n=1) had a score = 1, 5.24% (n=17) had a score = 2, 19.44% (n=63) had a score = 3. All of the patients whose NRS score ≤ 3 belonged to the non-NP group (0.41%, 6.97%, and 25.82%). There were 94.44% (n=306) patients with nutritional risk (>3 points). Among them, 92.62% (n=226) belonged to the non-NP group, and 92.62% (n=80) belonged to the NP group. Among the 99 patients (30.56%) with NRS scores = 4, there were 8.75% (n=7) with NP, and 37.70% (n=92) without NP; Among the 78 patients (24.07%) with NRS scores = 5, there were 25% (n=20) with NP, and 23.77% (n=58) without NP; Among the 43 patients (13.27%) with NRS scores = 6, there were 37.5% (n=30) with NP, and 5.33% (n=13) without NP; Among the 23 patients (7.11%) with NRS scores = 7, all of them (28.75%) belonged to the NP group. The incidence of nutritional risk in NP group was 100%.

To determine those that were significantly related to NP, we performed a multivariable logistic regression analysis of the correlation between risk factors and ACI in elderly patients. As shown in Table 2, the independent risk factors for NP in elderly patients with ACI were living alone (OR 4.723; CI 1.743~12.802; $P = .002$), initial NIHSS score (OR 1.441; CI 1.191~1.743; $P = .000$), NRS2002 score (OR 0.139; CI 0.087~0.223; $P = .000$), BMI (OR 1.586; CI 1.353~1.858; $P = .000$), a past pneumonia history (OR 0.073; CI 0.017~0.321; $P = .001$), AF (OR 0.129; CI 0.033~0.499; $P = .003$), CRP (OR 1.050; CI 1.017~1.085; $P = .003$), BUN (OR 0.603; CI 0.448~0.812; $P = .001$) and Cr (OR 1.036; CI 1.015~1.057; $P = .001$). Level of albumin was an independent protective factor of NP in elderly patients with ACI (OR 0.865; CI 0.750~0.999; $P = .048$).

Clinical outcomes between groups with and without NP in elderly patients with ACI are presented in Table 3. The NP group showed a longer duration of hospitalization (13.10 ± 7.02 days vs 11.78 ± 3.12 days; $P = .021$), worse effective outcome (62.50% vs 95.90%; $P = .000$), and high mortality (15% vs 0; $P = .000$).

4. Discussion

NP is a common complication in critically ill patients, particularly in patients who are intubated for more than 48 hours, and NP is responsible for significant in-hospital morbidity and mortality.^[9] The incidence of NP in the present study was 24.69%. In large-scale European prevalence of infection in intensive care (EPIC) study, the overall nosocomial pneumonia prevalence was 9.6%.^[10] This broad variation makes interstudy comparison complicated. In this study, the risk factors of NP in 70 years and over elderly patients with ACI were analyzed. We found that many factors, such as living alone, initial NIHSS score, malnutrition, a past pneumonia history, AF, CRP, and Renal function were associated with NP in elderly patients with ACI, and it correlated with pneumonia severity. Furthermore, NP significantly affected the clinical outcomes during hospitalization, as well as the outcomes after discharge.

Table 2
Multivariable logistic regression analysis.

	β values	SE values	Wald χ^2	OR (95%CI)	P
Living alone	1.552	0.509	9.312	4.723 (1.743~12.802)	.002**
Initial NIHSS score	0.365	0.097	14.170	1.441 (1.191~1.743)	.000**
NRS2002 score	-1.971	0.240	67.315	0.139 (0.087~0.223)	.000**
BMI (kg/m ²)	0.461	0.081	32.481	1.586 (1.353~1.858)	.000**
Pulmonary disease history	-2.614	0.753	12.036	0.073 (0.017~0.321)	.001**
AF	-2.048	0.690	8.806	0.129 (0.033~0.499)	.003**
CRP (mmol/L)	0.049	0.016	9.096	1.050 (1.017~1.085)	.003**
ALB (mmol/L)	-0.145	0.073	3.909	0.865 (0.750~0.999)	.048*
BUN (mmol/L)	-0.506	0.151	11.134	0.603 (0.448~0.812)	.001*
Creatinine (umol/L)	0.035	0.010	11.975	1.036 (1.015~1.057)	.001*

All data were expressed as mean \pm SEM.

AF = Atrial fibrillation, ALB = albumin, BMI = body mass index, BUN = blood urea nitrogen, CRP = C-reactive protein, NIHSS = National Institute of Health Stroke Scale, NRS2002 = nutritional risk screening 2002.

* $P < .05$.

** $P < .01$.

Symptoms and signs of pneumonia in elderly patients were unrepresentative, and it has more complications, higher incidence rate, and mortality. As in previous studies, elderly patients with NP had worse outcomes than those without NP both during hospitalization and after discharge. There are several ways in which NP can affect stroke outcomes. Immobilization because of medical complications and delays in rehabilitation may account for less recovery. Immunologic changes caused by NP may also enlarge stroke lesions and worsen clinical outcomes.^[11] Pneumonia is one of the main causes of morbidity and mortality in the elderly. The elderly population has exponentially increased in the last decades and the current epidemiological trends indicate that it is expected to further increase. Therefore, recognizing the special needs of older people is of paramount importance. The diagnosis of pneumonia in elderly patients can be challenging because its clinical presentation may be different from younger adults. Klapdor and colleagues suggested that CAP could be a different entity in the elderly because of an atypical clinical presentation, more severe symptoms and higher long-term mortality in comparison to younger patients. Therefore, an accurate evaluation of the appropriate site of care for elderly patients cannot rely only on severity assessment scores and other factors should also be considered.^[12] The Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) 2007 guidelines^[13] recommend evaluating subjective factors when deciding the setting of care: patients' ability to take oral medications, availability of outpatient support resources and caregivers in case of dependent patients, other medical or psychosocial needs (such as homelessness and poor functional status),

and lack of response to previous adequate empiric antibiotic therapy.^[14]

Living alone is where an older person lives alone in a household. Living arrangements depict familial and non-familial relationships with whom the older persons share/reside in the same household.^[15] In China, living arrangements for older people carry a special meaning. Among the 324 elderly patients at baseline, 37.04% (n = 120) were living alone. Under the influence of Confucianism, older Chinese traditionally co-reside with one or more of their married children; usually the oldest son. These trends have reduced household size, generated changes in living arrangements and increased the prevalence of 'empty nest families' (families in which older persons live alone and do not co-reside with adult children) in both urban and rural areas. A study examined the effect of living away from adult children on upward intergenerational monetary transfers by analyzing a 2006 survey of 19,947 persons aged 60 and above and selected from 20 provinces in China. Results indicate that living close to children, rather than co-residing with them, might be the primary living arrangement for older Chinese people in the foreseeable future.^[16] At the same time, as previous studies proved,^[17] having a spouse is the "greatest guarantee of support in old age".^[18] Marriage can bring health benefits through providing emotional intimacy, economic benefits, social control of behavior and more social integration,^[19] which will in turn influence the health outcome of the elderly. Here we found that living alone, independently of age, sex, socioeconomic, marital, and health status, was significantly associated with increased mortality overall among older persons living in China. Numerous studies show that elderly people living alone in the community are characterized by difficult living situations, limited resources and lack of support, and in need of medical services, financial subsidy and social and leisure activity settings. The lack of informal and formal support of family members and social services in monitoring health condition, medical appointments and caregiving^[20-22] are associated with poor self-management of chronic disease and increased risk of dying among the elderly who live alone. Older persons who live alone are recognized to be a vulnerable risk group in the population requiring special attention. Elderly people living alone have been described as an "at risk" group by the World Health Organization.^[23]

Neurological impairment in stroke patients was assessed by NIHSS score. The higher the score, the more serious the nerve damage, especially in patients with severe limb dysfunction who

Table 3
Outcomes of elderly patients with ACI.

	NP (n = 80)	non-NP (n = 244)	P
Hospitalization duration (d)	13.10 \pm 7.02	11.78 \pm 3.12	.021*
Outcome			.000**
Effective (%)	50 (62.50%)	234 (95.90%)	
Invalid (%)	30 (37.5%)	10 (4.10%)	
Death (%)	12 (15%)	0	.000**

All data were expressed as mean \pm SEM.

ACI = acute cerebral infraction, NP = nosocomial pneumonia.

* $P < .05$.

** $P < .01$.

needed long-term bed rest, was more likely to be associated with NP. The NIHSS is increasingly being used as the measure of stroke severity among patients with ischemic stroke. Our findings underscore the importance of using the NIHSS not only as a measure of stroke severity but also as part of an assessment for pneumonia risk. Stroke can cause varying degrees of dysphagia, a decrease in protective respiratory reflexes, and aspiration pneumonia when eating and drinking. Previous studies have shown that the NIHSS score is a risk factor for pneumonia.^[24] The higher the NIHSS score, the greater the likelihood of NP. The reason for this observation is that patients with high NIHSS scores often have a reduced level of consciousness or are on bed rest, and are prone to gastroesophageal reflux, leading to aspiration pneumonia.

Nutrition is one of the most important clinical factors influencing mortality due to infectious disease.^[25] Protein-energy homeostasis is a major determinant of healthy aging. It has been shown that lower protein intake was associated with higher frailty prevalence. Hospitalized older patients with better nutritional status and higher levels of ALB were less likely to develop into frailty. These nutrition-related biomarkers may be used for the evaluation of nutritional status and frailty in older patients.^[26] The BMI is widely used to define the baseline nutrition status.^[27] Several studies have revealed that underweight is associated with a risk of death due to pneumonia. Being underweight has also been reported as risk factor for the development of pneumonia.^[28–29] Wang J and colleagues suggested that The significant risk factors of ACI in malnourished patients older than 70 years were swallowing dysfunctions, disturbance of consciousness and reliance or half-reliance on feeding practices. The significant risk factors of malnutrition in patients with ACI were the decline in upper limb muscle strength, decline in the performance of various activities, loss of appetite and gastrointestinal symptoms.^[30] In addition, there were no reports regarding the relationship between nutritional risk and NP in elderly patients with ACI. In the present study, NRS2002 score was first introduced as a potential risk factor for readmission. We found that 360 of 324 patients (94.44%) were at nutritional risk, which was consistent with the reports from other studies.

A past history of pneumonia was one of the particularly influence factors. This strong association with a past history of pneumonia indicates that pneumonia is a reflection of a frail condition and the aggregate of many risk factors of contracting pneumonia.^[31] Patients with a previous history of pneumonia were at a higher risk of CAP in the current study, especially those whose initial episode occurred more than 2 years previously; in previous studies, the risk was higher for more recent episodes.^[32] In addition, elderly patients with recent episodes of pneumonia are less likely to recognize the symptoms and the seriousness of the illness, and therefore less likely to seek early treatment, averting hospital admission.

AF is the most common etiology of cardioembolic mechanism in patients with acute ischemic stroke.^[33] The prevalence of AF increases with age. As the population ages, the burden of AF increases. AF is associated with an increased incidence of mortality, stroke, and coronary events compared to sinus rhythm.^[34] AF is also an independent risk factor for stroke, especially in elderly persons. In the Framingham Study, the relative risk of stroke in patients with nonvalvular AF compared with patients with sinus rhythm was increased 2.6 times in patients aged 60 to 69 years, increased 3.3 times in patients aged 70 to 79 years, and increased 4.5 times in patients aged 80 to 89

years.^[35] A study in China examined AF is an independent risk factor for NP.^[36] Inflammation may be the mechanism with accumulating evidence that progression of comorbidities is associated with AF. Theoretically, inflammation plays an important role in AF patients.^[37] Various inflammatory markers such as CRP, tumor necrosis factor (TNF)- α , interleukin (IL)-2, IL-6, IL-8 have been demonstrated to be associated with AF.^[38]

Previous studies^[39] have shown that chronic kidney disease (CKD) not only leads to worse short-term prognosis in patients with acute stroke, but also affects long-term prognosis, and increases the risk of recurrence of stroke. The main causes of increased stroke incidence in CKD are as follow:^[40] Arteriosclerosis, cerebrovascular calcification, hemodynamic disorders, anemia and anticoagulant therapy have accelerated. The commonly used clinical CURB-65 score^[41] the assessment of the severity of NP and risk of death, can think of the BUN level is associated with the prognosis of NP positive. The main mechanisms of NP in renal insufficiency patients include immune deficiency, hypoproteinemia, dialysis factors, basic diseases and so on.^[42] The results of this study indicate that: the increase of BUN and Cr levels are independent risk factors for ACI in patients over 70 years with NP, which is consistent with previous reports.^[43]

ACI combined with NP is correlated with the prognosis. Domestic team found that:^[44] ACI patients with NP are older, more severe; more suffering from heart failure, AF, myocardial infarction; more suffering from disorder of consciousness since onset. NP is an independent prognostic factor for long-term unfavorable outcome and for long term mortality in patients with ACI. In this study, non-NP patients were better than those in group NP ($P < .01$) in terms of treatment and prognosis, and the 2 conclusions were consistent.

This study was designed as a single center retrospective study. However, the study had some limitations that should be acknowledged. As a retrospective study, all data were obtained from the patients' medical records, and the cases could be excluded without complete information. There was still a possibility of selection bias and generalization of the findings to clinical fields should be cautious.

First, as a secondary comprehensive hospital located in the suburb region of Tianjin (China), the vast majority of inpatients in our hospital are elderly. As the local condition, the economic level and education level of mostly elder patients' family was lower, and the medical economy burden of the poverty family. That also means there is a lack of awareness about the right nutrition and nursing care for older people; Second, patient age is reported to be a risk factor of mortality due to pneumonia. Many severity assessment systems for pneumonia incorporate the patient age.^[45] Age-related muscle atrophy due to prolonged immobilization, pneumonia-related hypoxia and systemic inflammation have been proposed to be the main pathogenic mechanisms.^[46] However, all of the patients in this study are 70 years old and over, We found that age did not have a significant influence on the risk factors of NP in elderly patients with ACI; Third, traditional indicators of primary infection include high white blood cell and neutrophil counts, but these indicators are not typically diagnostic. According to a previous study, there were no significant differences in leukocyte or neutrophil counts between patients with and without infection at admission, suggesting that the predictive value of leukocyte and neutrophil counts for infection is limited,^[47] which is consistent with the results of our study. Our single-factor analysis found that WBC counts differed between the NP and non-NP groups, but the

results of the multivariate analysis did not support the predictive values of these risk factors for NP. This apparent discrepancy may be related to the small number of cases examined. And according to the elderly patients, immune function declines after stroke may lead to lower WBC levels; next, the timing of admission and duration of hospitalization may have led to bias. We included elderly patients with ACI who were evaluated within 3 days of developing symptoms. Because NP mainly occurs as early as the first 48 hours, some events may have been missed. However, the established warning system for early symptom surveillance played an effective role in case finding and identification of suspected cases. Thus, these biases were within acceptable ranges. Even though we excluded patients with active infections before admission, we cannot rule out bias from undiagnosed infections that occurred before admission; finally, the factors on mechanical ventilation should be considered. The traditional risk factors for NP, such as severe and lingering illnesses, tracheal intubations and/or mechanical ventilation were not involved in our case because these confounding factors had been eliminated as exclusion criteria. Therefore, the impact of mechanical ventilators does not seem to be of much significance. However, because ventilator-associated pneumonia is known to present with different characteristics from Pneumonia, the effects of mechanical ventilation should be considered before generalizing our results to the clinical field.^[48] Therefore, more multicenter RCTs with high quality, large sample, and adequate follow up are required for further verification.

5. Conclusion

To sum up, we identified significant risk factors for NP in elderly patients with ACI, including living alone, initial NIHSS score, malnutrition, a past pneumonia history, AF, CRP, and Renal function were associated with NP in elderly patients with ACI. In our study, the clinical course was worse and the duration of hospital stay was longer in NP patients than in non-NP patients.

Author contributions

Data Curation: Yun Xianghua, Chen Jun, Li Min.

Methodology: Yun Xianghua.

Writing - Original Draft: Yang NanZhu.

Writing - Review & Editing: Li Xin.

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