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Original Article

Analysis of etiology, risk factors and prognosis of pulmonary infection in elderly patients with acute cerebral infarction

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Abstract: Objective: The goal of this study was to investigate the etiology, risk factors, and prognosis of pulmonary infection in elderly patients with acute cerebral infarction (ACI). Methods: A total of 758 elderly patients with ACI were divided into an infected group (n = 254) and a non-infected group (n = 504), according to bacteriologic analysis retrospectively. Distribution of pathogens was observed in the infected group. Clinical data, length of stay (LS), and 28-day mortality rates were compared between the two groups, and a K-M curve was plotted for analysis of survival. Logistic multivariate regression analysis was used for analyzing independent risk factors for pulmonary infection. Results: Significant differences were found regarding age, history of diabetes, smoking and alcoholism, consciousness disorders, dysphagia, and invasive nursing procedures, and albumin levels (all $P<0.05$). A total of 322 microbiological strains were isolated from 254 patients, mainly Gram-negative bacteria (64.92%). Both the LS and 28-day mortality rate were significantly greater in the infected group (both $P<0.05$). Logistic multivariate analysis found age, consciousness disturbance, dysphagia, invasive manipulation, albumin levels, and LS to be independent risk factors for pulmonary infection. Conclusion: Risk factors for complication with pulmonary infection in patients with ACI include age, consciousness disturbances, dysphagia, invasive procedures, albumin levels, and length of hospital stay.

Keywords: Acute cerebral infarction, pulmonary infection, etiology, risk factors, prognosis analysis

Introduction

Acute cerebral infarction (ACI), also known as acute ischemic stroke, is caused by the occurrence of arterial atherosclerosis, which leads to vascular stenosis and occlusion, gradually resulting in insufficient blood supply to the brain [1, 2]. Clinically, ACI is the most common high-risk disease in the elderly, characterized by "three highs": high incidence, high disability rate, and high mortality [3]. ACI is currently recognized as a global public health problem, ranking as the second most global cause of death in 2016, and accounting for more than 5.6 million deaths yearly [4].

Complications are common in the clinical management of ACI, and the most frequent one is infection [5]. In patients with ACI, the incidence of infection has been estimated at 21-65%, with the most common type being pulmonary infection [6, 7]. This has been attributed to a decline in patients' immunity and respiratory defense function. Once established, infections rapidly deteriorate patients' conditions and complicate management, hindering treatment of the primary disease [8]. Furthermore, the mortality rate of patients with ACI and infection has been estimated to be as high as 70% within 4 years, while that of non-infected patients remains at only 20% [9]. Many risk factors have been described for pulmonary infection in patients with ACI, yet these associations remain rather unclear. Therefore, this study aimed to evaluate risk factors for pulmonary infection in patients with ACI and provide a reference for clinicians in regard to prevention and empirical use of antibiotics.

Table 1. Assignment table

Factor	Value
Infection	Infected = 1, non-infected = 0
Age	≥65 = 1, <65 = 0
Diabetes	Yes = 1, No = 0
Smoking history	Yes = 1, No = 0
Alcoholism history	Yes = 1, No = 0
Conscious disturbance	Yes = 1, No = 0
Dysphagia	Yes = 1, No = 0
Invasive procedure	Yes = 1, No = 0
Albumin	≥30 = 1, <30 = 0

Materials and methods

General information

This study retrospectively analyzed clinical and laboratory data of 758 patients with ACI treated in The Nursing College of Zhengzhou University from May 2014 to September 2016. According to results from the bacteriologic analysis of sputum cultures, patients were divided into an infected group (n = 254) and a non-infected group (n = 504). This study was approved by the medical ethics committee of The Nursing College of Zhengzhou University. Informed consent was obtained from all individuals included in this study.

Inclusion and exclusion criteria

Inclusion criteria: All patients were diagnosed with ACI by CT and MRI; onset within 14 days; body temperature ≥38°C; peripheral blood leukocytes $\geq 1*10^{10}$/L; presence of bilateral dry and moist rales in the lungs with cough, sputum, and other related symptoms; presence of pathogenic bacteria in sputum cultures; availability of the patients' complete medical records.

Exclusion criteria: Patients with brain dysfunction caused by primary and secondary intracranial tumors, and history of craniocerebral injury or epilepsy.

Sample collection and microbiological analysis

Patients were instructed to rinse the mouth repeatedly 3 times with saline before eating in the morning, and to cough up sputum in the deep, which was collected into a sterile specimen box and immediately sent to the laboratory of the hospital for sputum culture. For patients who were unconscious, lethargic, or intubated, suction catheter or bronchoscopes were used to extract deep secretions for examination. Sputum culture results were collected for statistical analysis.

Collection of medical records

Clinical data of all patients was collected, including gender, age, history of diabetes, hypertension, smoking, alcohol abuse, and chronic obstructive pulmonary disease, as well as the presence of disturbances in consciousness, dysphagia, and invasive procedures, along with albumin levels, and bedridden time.

Observation indicators

Clinical data and length of stay (LS) were compared between the two groups. The distribution of pathogenic bacteria was observed in the infected group. The 28-day mortality was compared between the groups, and a K-M curve was plotted for the analysis of survival. Logistic multivariate regression analysis was performed in order to evaluate independent risk factors for pulmonary infection in patients with ACI (**Table 1**).

Statistical analysis

SPSS 20.0 software was used for statistical analysis, and GraphPad Prism 7 was used for image drawing. Quantitative data are expressed as the mean ± standard deviation ($\bar{x}$ ± SD). Paired t test was used for intra-group comparisons, while the t test for independent samples was used for inter-group comparisons, represented by t. Enumeration data are expressed as number of cases/rate (n/%) and assessed with the Chi-square test (χ^2). A K-M curve was plotted for the analysis of patient survival, and the results were tested by log-rank. Logistic multivariate regression analysis was performed to assess independent risk factors for pulmonary infections in patients with ACI. Differences were considered statistically significant when $P<0.05$.

Results

Comparison of clinical data

No statistically significant differences were found regarding gender, history of hyperten-

Table 2. Comparison of clinical information (n, %)

	Infected group	Non-infected group	X^2	P
Gender			1.596	0.207
Male	139 (54.72)	300 (59.52)		
Female	115 (45.28)	204 (40.48)		
Age (year)			12.465	<0.001
≥65	182 (71.65)	295 (58.53)		
<65	72 (28.35)	209 (41.47)		
Diabetes			23.002	<0.001
Yes	198 (77.95)	305 (60.52)		
No	56 (22.05)	199 (39.48)		
Hypertension history			0.055	0.816
Yes	212 (83.46)	424 (84.13)		
No	42 (16.54)	80 (15.87)		
Smoking history			27.800	<0.001
Yes	192 (75.59)	282 (55.95)		
No	62 (24.41)	222 (44.05)		
Alcoholism history			6.047	0.014
Yes	50 (19.69)	65 (12.90)		
No	204 (80.31)	439 (87.10)		
Conscious disturbance			22.777	<0.001
Yes	165 (64.96)	235 (46.63)		
No	89 (35.04)	269 (53.37)		
Dysphagia			20.129	<0.001
Yes	188 (74.02)	289 (57.34)		
No	66 (25.98)	215 (42.66)		
COPD			0.132	0.716
Yes	130 (51.18)	265 (52.58)		
No	124 (48.82)	239 (47.42)		
Invasive procedure			70.651	<0.001
Yes	92 (36.22)	54 (10.71)		
No	162 (63.78)	450 (89.29)		
Albumin (g/L)			9.960	0.002
≥30	88 (34.65)	120 (23.81)		
<30	166 (65.35)	384 (76.19)		
Bedridden time (d)			0.570	0.450
≥14	148 (58.27)	308 (61.11)		
<14	106 (41.73)	196 (38.89)		

Note: COPD, chronic obstructive pulmonary disease.

sion, or chronic obstructive pulmonary disease or bedridden time between the infected and non-infected groups (all P>0.05). In contrast, significant differences were ascertained concerning age, history of diabetes, smoking and alcoholism, presence of consciousness disturbances, dysphagia, invasive nursing procedures, and albumin levels (all P<0.05, **Table 2**).

Distribution of pathogens in infected patients

Microbiological analysis of sputum cultures revealed 254 patients were infected and 504 patients were not infected, with an infection rate of 33.51%. A total of 322 microbiological strains were isolated from the 254 patients, of which 209 strains (64.92%) were Gram-negative bacteria, 101 (31.36%) were Gram-positive bacteria, and 12 (3.72%) were fungal strains (**Table 3**).

LS and the 28-day mortality rates

LS was found to be greater in the infected group (15.92±3.54 d) than in the non-infected group (8.78±2.83 d; t = 30.069, P = 0.001). Additionally, the 28-day mortality was significantly higher in the infected group than in the non-infected group (P<0.001, **Table 4**, **Figure 1**).

Risk factor analysis

Indicators with significant differences in clinical data were collected for logistic multivariate regression analysis, and it was found that age (OR = 0.563, 95% CI: 0.395-0.804), disturbance of consciousness (OR = 2.218, 95% CI: 1.581-3.111), dysphagia (OR = 2.066, 95% CI: 1.445-2.956), invasive procedures (OR = 4.909, 95% CI: 3.271-7.366), albumin levels (OR = 1.827, 95% CI: 1.111-3.006), and LS (OR = 1.347, 95% CI: 1.347-1.507) were independent risk factors for pulmonary infection in patients with ACI in our samples (**Table 5**).

Discussion

As a common disease in the elderly, the incidence of ACI in China has been rising in the last 30 to 40 years, with cerebrovascular disease becoming the deadliest illness [10, 11]. At present, the treatment of ACI is centered on “surgery plus drugs”, yet complications are still very frequent, especially in elderly populations.

Table 3. Distribution of pathogens

Pathogenic bacteria	Number	Constituent ratio (%)
Gram-negative bacteria		64.92
Escherichia coli	65	20.19
Klebsiella pneumoniae	52	16.15
Acinetobacter baumannii	49	15.22
Pseudomonas aeruginosa	31	9.63
Burkholderia cepacia	12	3.73
Gram-positive bacteria		31.36
Staphylococcus aureus	52	16.15
Staphylococcus haemolyticus	43	13.35
Staphylococcus epidermidis	6	1.86
Fungi		3.72
Candida albicans	7	2.17
Candida tropicalis	5	1.55
Total	322	100.00

Table 4. The 28-day mortality rate of two group (n, %)

Group	7 d	14 d	21 d	28 d
Infected group (n = 254)	25 (9.84)	48 (18.90)	50 (19.69)	63 (24.80)
Non-infected group (n = 504)	19 (3.77)	32 (6.35)	40 (7.94)	50 (9.92)
χ^2	11.586	29.671	24.158	30.173
P	0.001	<0.001	<0.001	<0.001

Deterioration is often accelerated by the immunological decline and nutritional-metabolic imbalances found in the elderly, contributing to increased mortality in these patients [12-14]. In particular, elderly patients with ACI are prone to nosocomial infections, among which pulmonary infections are the most common, which in turn are the main cause for increased mortality in these patients [15, 16]. Therefore, investigating the pathogenic features and risk factors for pulmonary infections in elderly patients with ACI is essential to the treatment and prevention of these cases.

In this study, retrospective analysis on 758 patients with ACI found 33.51% (n = 254) of the cases to be complicated with pulmonary infections, consistent with the report by Li et al. [17]. Various factors may promote the prominence of pulmonary infections in this population: prolonged bedridden time favors the accumulation of blood in the alveoli, which impairs elimination of sputum and thus facilitates infection. In addition, the abuse of G-bacterium antibiotics in recent years has led to increased incidence of infections by Gram-negative bacteria, including Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii, along with severe drug resistance, which also worsens prognosis for patients with pulmonary infections [18]. Our evaluation of the pathogenic bacteria found in the sputum of infected patients revealed the main pathogens to be Gram-negative bacteria, in harmony with the findings of Liu et al. [19]. This evidence may support the prophylactic use of broad-spectrum antibiotics covering anti-Gram-negative bacteria. Notably, a small proportion of the pathogenic strains found in our study were fungi, mainly found in the oldest patients. Indeed, aging patients may have varying degrees of degenerative changes in various tissues and organs, with particular compromise of the immune system. In addition, as the respiratory mucosal barrier function declines, long-term bed rest and antibiotic abuse lead to alterations in the respiratory flora of these patients, facilitating fungal infections [20, 21].

Multivariate logistic regression analysis was performed on the variables which showed differences between the infected and non-infected groups; age, disturbances in consciousness, dysphagia, invasive procedures, albumin levels, and LS were found to be independent risk factors for pulmonary infections in patients with ACI. LS is a well-known risk factor for infection. Furthermore, infection tends to demand additional in-hospital procedures, leading to a vicious circle that aggravates the patient's condition [22]. Additionally, patients subjected to invasive procedures showed a probability for developing lung infections 4.9 times higher than those who did not undergo invasive procedures. These techniques tend to damage the skin and mucosal barriers, facilitating invasion by pathogens. Moreover, repeated oxygenation, sputum aspiration and gastric intubation increase damage to the trachea and bronchus, resulting in weakened autologous clear-

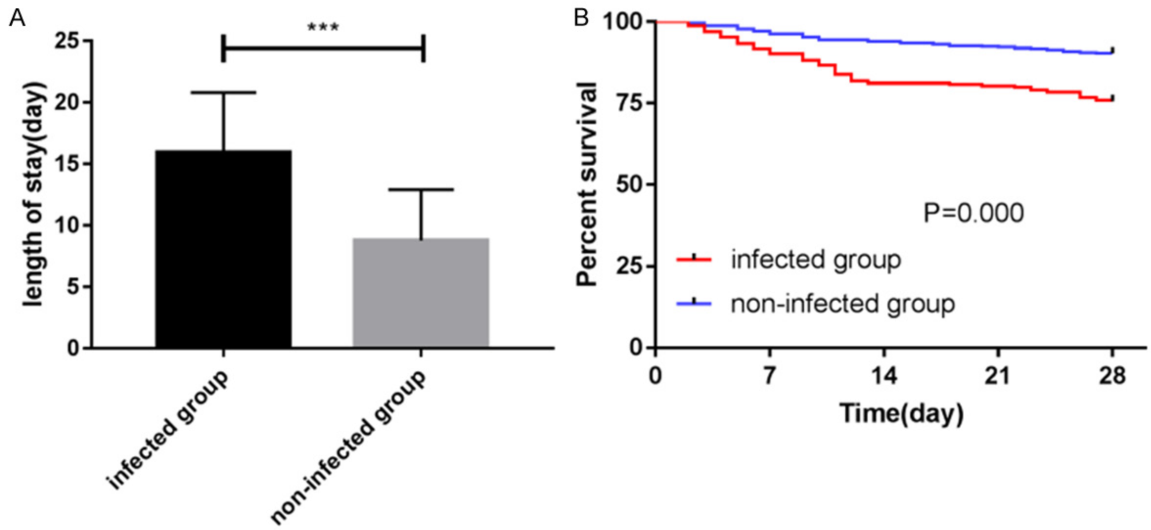

Figure 1. Comparison of length of hospital stay and 28-day mortality. A. Length of hospital stay of the infected group and the non-infected group. ***P<0.001. B. 28-day mortality of the infected group and the non-infected group (P<0.001).

Table 5. Logistic multivariate regression analysis

Factors	β	S.E.	Wals	Sig	Exp (β)	95% CI	
Age	-0.574	0.181	10.035	0.002	0.563	0.395	0.804
Diabetes	-0.222	0.178	1.553	0.213	0.801	0.564	1.136
Smoking history	-0.325	0.171	3.614	0.057	0.723	0.517	1.010
Alcoholism history	-0.060	0.311	0.037	0.848	0.942	0.513	1.732
Conscious disturbance	0.797	0.173	21.306	<0.001	2.218	1.581	3.111
Dysphagia	0.726	0.183	15.792	<0.001	2.066	1.445	2.956
Invasive procedure	1.591	0.207	59.034	<0.001	4.909	3.271	7.366
Albumin	0.603	0.254	5.635	0.018	1.827	1.111	3.006
Length of stay	0.354	0.029	151.293	<0.001	1.425	1.347	1.507

ance of tracheal mucociliary [23]. Infection cases are common in the elderly with weaker body function and immunity. Patients were found with alterations in consciousness disturbance that had a higher probability of lung infection. Disturbance of consciousness rendered the patients more vulnerable to aspiration of contaminated gases, pulmonary congestion, and thereby infection [24, 25]. This was compounded by difficulties with swallowing, which favored reflux of food particles and pharyngeal secretions into the airways of the patient, further increasing the probability of aspiration infection [26]. Furthermore, dysphagia restricts daily nutritional intake which is often impossible to replenish, leading to the reduction of patients' albumin levels.

Analysis of survival from the 28-day mortality curve ascertained the mortality rate of the infected group to be significantly higher than that of the non-infected group. This was attributed to the aggravation of the patients' conditions after the occurrence of infection, which, in conjunction with the aforementioned related factors, lead to increased mortality.

There are some limitations to this report. As a retrospective analysis, this study is susceptible to result bias. Furthermore, the results should be verified in larger studies. We expect to corroborate the findings in more comprehensive studies in the future.

In conclusion, key risk factors for pulmonary infection in patients with ACI were identified, including age, consciousness disturbances, dysphagia, invasive procedures, albumin levels, and LS.

Disclosure of conflict of interest

None.

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