A Risk Factor Analysis of Cognitive Impairment in Elderly Patients with Chronic Diseases in a Chinese Population

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Background: This study analyzed the risk factors of cognitive impairment (CI) in elderly patients with chronic diseases. The activities of daily living (ADL), global deterioration scale (GDS), Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment Scale (MoCA), patient-generated subjective global assessment (PG-SGA), and mini nutritional assessment (MNA) were performed to analyze the differences between the 2 groups. Logistic regression analysis was conducted for risk factors of CI in elderly patients with chronic diseases.

Material/Methods: In total of 385 elderly patients with chronic diseases were selected and assigned into CI and normal groups. The activities of daily living (ADL), global deterioration scale (GDS), Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment Scale (MoCA), patient-generated subjective global assessment (PG-SGA), and mini nutritional assessment (MNA) were performed to analyze the differences between the 2 groups. Logistic regression analysis was conducted for risk factors of CI in elderly patients with chronic diseases.

Results: There were differences in age, education level, type 2 diabetes mellitus, multifocal cerebral infarction, hearing, and eyesight between CI and normal groups. Patients in the CI group showed more CD4\(^+\) cells, more admission times, and higher GDS scores than the normal group. Also, MMSE and MoCA scores revealed differences in total score, directive force, attention and calculating ability, language, delayed memory, reading comprehension, writing, and visual-spatial ability between the 2 groups. The number of B and CD8\(^+\) cells, ADL, and MNA scores were protective factors, while cerebral infarction history, number of CD4+ cells, admission times, GDS score, and age were risk factors of CI in elderly patients with chronic diseases.

Conclusions: Our study provides evidence that cerebral infarction history, number of CD4+ cells, admission times, GDS score, and age are risk factors of CI in elderly patients with chronic diseases.

MeSH Keywords: Chronic Disease • Mild Cognitive Impairment • Risk Factors

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Background

Chronic diseases are a severe social issue and the leading cause of death in the modern era, most of which are regarded as the result of physical inactivity [1]. The elderly are more prone to chronic diseases and mobility limitation than the young, often with concurrent cognitive and mental disorders, which make many elderly patients need constant care and attention [2]. In general, hypertension (76.4%), dyslipidemia (54.2%), arrhythmia (38.5%), arthritis (36.2%), and coronary heart disease (34%) are the 5 most common chronic diseases [3]. According to the World Health Organization (WHO), there were about 350 million elderly people around the world in 1975 and this figure will reach more than 1.1 billion by 2025 [4]. A recent study has shown that around 80% of adults over 65 years of age have at least 1 chronic disease, and 50% have more than 2 chronic diseases [5]. A previous study demonstrated that chronic kidney disease is associated with elevated risk for dementia in elderly people with poor executive function, cognitive function, memory and language ability [6], suggesting associations between chronic diseases and cognitive impairment (CI).

CI can lead to dementia and is associated with decreased quality of life, poor prognosis, and high prevalence of hypertension [7]. Identified risk factors for CI include age, sex, family history, and educational background, as well as risk factors of cerebrovascular disease like diabetes and hypertension [8]. Drugs with anticholinergic properties are considered another important risk factor for CI in the elderly [9]. One study reported that CI is associated with elevated microalbumin excretion and large artery stiffness in newly diagnosed, but untreated, hypertensive patients [10]. It is noteworthy that type 2 diabetes mellitus is a widely-recognized risk factor for CI and dementia in the elderly, and a study reported that the increased number of diabetic patients with CI is accompanied by an increased number of elderly patients with type 2 diabetes mellitus [11]. Furthermore, c-reactive protein (CRP) is one of the most commonly reported biomarkers of systemic inflammation, and rising CRP levels measured at middle-old adulthood were reported to be correlated with late-life poorer cognitive performance and to a steeper decline in cognitive function [12]. CI is commonly seen in a variety of diseases; for example, patients with carotid artery occlusion (CAO) and ipsilateral transient ischemic attack (TIA) were found to have lasting CI, regardless of the recovery of focal neurological deficits [13]. Although many previous studies have focused on risk factor analysis of CI, few have studied the risk factors for CI, particularly in elderly patients with chronic diseases. In the present study, we investigated the risk factors of CI in elderly patients with chronic diseases to provide a theoretical foundation for the early prevention and treatment of the disease.

Material and Methods

Subjects

Between February 2015 and June 2016, 385 elderly patients (321 males and 64 females; mean age 81.8±5.1 years) were selected from among 689 elderly patients with chronic diseases who received treatment in the Geriatric Department of Anhui Provincial Hospital. The clinicopathological characteristics of all patients were recorded. According to diagnosis, there were: 194 patients with hypertension, 200 with type 2 diabetes mellitus, 77 with hypercholesterolemia, 124 with hyperuricemia, 150 with multifocal cerebral infarction, 111 with chronic obstructive pulmonary disease, 148 with cardiac insufficiency, 149 with renal insufficiency, 310 with hearing loss, and 357 with visual loss. Each chronic disease was strictly diagnosed by mid-level or high-level experienced specialists. We included patients with a history of chronic disease of over 2 years and patients with chronic pain derived from chronic diseases who had high pain scores (>2 points) evaluated by numerical rating scale (NRS). Other inclusion criteria were: (1) All patients were over 65 years old; (2) Patients received education of junior high school degree or above; and (3) Patients had good cooperation during the research. Exclusion criteria were: (1) Patients with mental illness in the active stage or emotional instability; (2) Patients with obvious cerebral trauma, stroke sequelae or severe organ failure; and (3) Patients receiving acute management of chronic diseases. Based on the cognitive function evaluated by clinical dementia rating (CDR), patients were assigned into the CI group or the normal group. This study was approved by the Ethics Committees of Anhui Provincial Hospital. Informed consent was obtained from all enrolled individuals.

Data collection

Clinical information of all patients was collected, including age, sex, education level, marital status, lifestyle, smoking history, drinking history, dietary structure, admission times, and infection history in recent months. Because of different education systems and study methods in all elderly patients, patients were divided into a group with education ≤8 years and a group with education >8 years, based on the number of years that patients attended school, which was close to the division between junior high school and below versus senior high school and above. Using information provided by patients or family members, patients were subdivided into a smoking history group and a non-smoking history group, a drinking history group and a non-drinking history group, and a high-meat diet group and a low-meat diet group. The admission times were recorded as the total admission times of either chronic disease-related or unrelated disease since the day on which they were diagnosed as having a chronic disease. Infection in recent months was defined as infection occurring as early as January.
Records of baseline characteristics

Clinical signs and measurable indicators such as height, weight, blood pressure, pain, waistline, hip circumference, biceps circumference, and triceps skinfold thickness (TSF) were collected by nurses or physicians in strict accordance with standardized principles of residency. Blood parameters were measured with an automatic hematology analyzer (BCC-3000B; Sande Medical Appliances, Nanjing, Jiangsu, China), including white blood cell (WBC) count, lymphocyte count, blood platelet count (BPC), hemoglobin content, prealbumin, albumin, CRP, creatinine, urea nitrogen, cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C), immune globulin, and T, B, and natural killer cells (NK) cell subsets.

Comprehensive geriatric assessment

A general assessment scale, a neuropsychological assessment scale, and a nutritional status assessment scale were used to evaluate the activities of daily living (ADL), the degree of overall cognitive function, neuropsychological status, and nutritional status. Quality control in all evaluation scales was performed before investigation. The whole investigation was conducted by trained and qualified doctors (bachelor or postgraduate) using uniform questionnaires and standardized tests. A pre-investigation was performed with 2 subjects randomly selected from all patients to discuss and solve problems during pre-investigation. The kappa coefficient was 0.81 for questionnaire results, and the information bias caused by investigators was expected to be controllable. For some patients with memory impairment, accompanying family members assisted during investigation to limit recall bias.

The ADL scale [14] was applied to assess the ability to perform activities of daily living (ADL). If the ADL score was >3 points in 2 or more sub-items or if the total ADL score was >22 points, patients were confirmed to have deterioration of ADL. Based on their performance in cognitive domains and social life, the global deterioration scale (GDS) was used to evaluate the degree of CI [15].

The clinical dementia rating (CDR) scale [16] was used to assess the cognitive and functional performance of all patients and to screen for dementia. The Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment Scale (MoCA) [17] were also used to evaluate cognitive performance. To avoid the “ceiling effects”, patients with full scores on the MMSE or suspicious actions were retested. Patients with MMSE scores ≥26 points were considered as normal. Hamilton’s Depression Rating Scale (24-items; HAMD-24) was used to screen for the presence of depressive symptoms, which might eliminate pseudodementia caused by depression.

The nutritional status of elderly patients was assessed with patient-generated subjective global assessment (PG-SGA) and mini-nutritional assessment (MNA) scales [18]. In accordance with the medical history and related information, nutritional conditions of patients were classified into good nutrition, mild malnutrition, moderate malnutrition, and severe malnutrition. The MNA was also used to reduce the retrospective bias for objectivity and reliability.

Statistical analysis

All data were analyzed with SPSS version 20.0 software (SPSS Inc, Chicago, IL). Measurement data are expressed as mean ± standard deviation (mean ±SD). Descriptive analysis of variable data was performed. Comparisons of data between 2 groups were conducted using the independent-samples t test. P<0.05 was defined as being statistically significant. Correlation between enumeration data and risk factors was analyzed with the chi-square test. Polytomous variables were analyzed using Kruskal-Wallis rank sum test. Logistic regression analysis was used for multivariate analysis of risk factors for CI in elderly patients with chronic diseases. P<0.05 was considered as statistically significant. The kappa statistic was used to assess the level of agreement in questionnaire results.

Results

Enumeration data between the CI group and the normal group in elderly patients with chronic diseases

After patients were assigned into 2 groups according to their cognitive function, enumeration data was compared, revealing significant differences in age and education level between CI group and the normal group (both P<0.05). However, there was no significant difference between the 2 groups in sex, marital status, living pattern, sleeping quality, smoking history, drinking history, or dietary structure (all P>0.05). In terms of medical history, the 2 groups differed from each other in type 2 diabetes mellitus, multifocal cerebral infarction, hearing ability, and eyesight (all P<0.05). No obvious differences were found between the 2 groups in recent infection history, pain, hypertension, hypercholesteremia, hyperuricemia, chronic obstructive pulmonary disease, cardiac function, or renal function (all P>0.05) (Table 1).

Measurement data in the CI group and normal group in elderly patients with chronic diseases

Table 2 shows that patients in the CI group were older, had more CD4+ cells, more admission times, and higher GDS score than in the normal group (all P<0.05). On the other hand, there were fewer CD8+ cells and less B cells, and lower ADL and MNA scores in the CI group than in the normal group (all P<0.05).
Table 1. Comparison of enumeration data between the CI group and the normal group in elderly patients with chronic diseases.

|                                | CI group (n=163) | Normal group (n=222) | P     | OR    | 95% CI          |
|--------------------------------|------------------|----------------------|-------|-------|-----------------|
| Gender                         |                  |                      | 0.598 | 0.865 | 0.504–1.484     |
| Male                           | 134              | 187                  |       |       |                 |
| Female                         | 29               | 35                   |       |       |                 |
| Age (years)                    |                  |                      | <0.001| 2.441 | 1.608–3.705     |
| >81                            | 106              | 96                   |       |       |                 |
| ≤81                            | 57               | 126                  |       |       |                 |
| Education level (years)        |                  |                      | 0.026 | 1.592 | 1.057–2.397     |
| ≤8                             | 81               | 85                   |       |       |                 |
| >8                             | 82               | 137                  |       |       |                 |
| Marital status                 |                  |                      | 0.683 | 1.090 | 0.720–1.650     |
| Married                        | 101              | 133                  |       |       |                 |
| Unmarried                      | 62               | 89                   |       |       |                 |
| Living pattern                 |                  |                      | 0.304 | 1.316 | 0.779–2.226     |
| Companied                      | 136              | 176                  |       |       |                 |
| Alone                          | 27               | 46                   |       |       |                 |
| Sleeping quality               |                  |                      | 0.174 | 1.325 | 0.883–1.988     |
| Poor                           | 105              | 92                   |       |       |                 |
| Good                           | 58               | 130                  |       |       |                 |
| Smoking history                |                  |                      | 0.801 | 0.942 | 0.592–1.500     |
| Yes                            | 40               | 58                   |       |       |                 |
| No                             | 123              | 168                  |       |       |                 |
| Drinking history               |                  |                      | 0.061 | 0.676 | 0.449–1.018     |
| Yes                            | 85               | 137                  |       |       |                 |
| No                             | 78               | 85                   |       |       |                 |
| Dietary structure              |                  |                      | 0.061 | 1.509 | 0.981–2.323     |
| High-meat diet                 | 61               | 63                   |       |       |                 |
| Low-meat diet                  | 102              | 159                  |       |       |                 |
| Infection history within one month |        |                      | 0.971 | 1.008 | 0.647–1.571     |
| Yes                            | 48               | 65                   |       |       |                 |
| No                             | 115              | 157                  |       |       |                 |
| Pain                           |                  |                      | 0.516 | 1.197 | 0.695–2.059     |
| Yes                            | 29               | 34                   |       |       |                 |
| No                             | 134              | 188                  |       |       |                 |
| Condition                                | CI group (n=163) | Normal group (n=222) | P      | OR      | 95% CI         |
|------------------------------------------|------------------|----------------------|--------|---------|----------------|
| Hypertension                             |                  |                      | 0.206  | 0.770   | 0.513–1.155    |
| Yes                                      | 76               | 118                  |        |         |                |
| No                                       | 87               | 104                  |        |         |                |
| Type 2 diabetes mellitus                 |                  |                      | 0.003  | 1.853   | 1.229–2.794    |
| Yes                                      | 99               | 101                  |        |         |                |
| No                                       | 64               | 121                  |        |         |                |
| Hypercholesteremia                       |                  |                      | 0.381  | 1.251   | 0.758–2.067    |
| Yes                                      | 36               | 41                   |        |         |                |
| No                                       | 127              | 181                  |        |         |                |
| Hyperuricemia                            |                  |                      | 0.320  | 1.244   | 0.808–1.914    |
| Yes                                      | 57               | 67                   |        |         |                |
| No                                       | 106              | 155                  |        |         |                |
| Multifocal cerebral infarction           |                  |                      | 0.004  | 1.827   | 1.206–2.770    |
| Yes                                      | 77               | 73                   |        |         |                |
| No                                       | 86               | 149                  |        |         |                |
| Chronic obstructive pulmonary disease    |                  |                      | 0.171  | 1.362   | 0.874–2.124    |
| Yes                                      | 53               | 58                   |        |         |                |
| No                                       | 110              | 164                  |        |         |                |
| Cardiac insufficiency                    |                  |                      | 0.179  | 1.329   | 0.878–2.012    |
| Yes                                      | 69               | 79                   |        |         |                |
| No                                       | 94               | 143                  |        |         |                |
| Renal insufficiency                      |                  |                      | 0.537  | 1.139   | 0.753–1.725    |
| Yes                                      | 66               | 83                   |        |         |                |
| No                                       | 97               | 139                  |        |         |                |
| Hearing loss                             |                  |                      | 0.011  | 2.01    | 1.165–3.467    |
| Yes                                      | 141              | 169                  |        |         |                |
| No                                       | 22               | 53                   |        |         |                |
| Eyesight diminution                      |                  |                      | 0.006  | 3.652   | 1.358–9.823    |
| Yes                                      | 158              | 199                  |        |         |                |
| No                                       | 5                | 23                   |        |         |                |

CI – cognitive impairment; OR – odd ratio; 95% CI – 95% confidence interval.
Table 2. Comparison of measurement data between the CI group and the normal group in elderly patients with chronic diseases.

|                        | CI group (n=163) | Normal group (n=222) | t/z   | P   |
|------------------------|------------------|----------------------|-------|-----|
| Height (cm)            | 168.88±14.201    | 168.72±16.424        | 0.102 | 0.919 |
| Weight (Kg)            | 62.29±14.750     | 63.70±15.581         | -0.896| 0.371 |
| Age (years)            | 83.28±3.498      | 79.82±5.629          | 6.931 | <0.001|
| BMI (Kg/m²)            | 21.67±3.444      | 22.19±3.363          | -1.51 | 0.132 |
| Systolic pressure (mmHg)| 139.32±15.741   | 142.27±19.618        | -1.636| 0.103 |
| Diastolic pressure (mmHg)| 102.40±20.798  | 104.14±24.456        | -0.75 | 0.453 |
| Pulse pressure (mmHg)  | 36.92±14.888     | 38.14±13.529         | -0.75 | 0.453 |
| Waistline (cm)         | 79.81±10.090     | 78.81±9.098          | 0.518 | 0.605 |
| Biceps circumference (cm)| 25.72±2.026    | 26.18±1.874          | -1.96 | 0.051 |
| TSF (cm)               | 2.06±0.471       | 2.07±0.359           | -0.445| 0.656 |
| Leukocyte (×10⁹/L)     | 6.91±1.944       | 6.76±1.934           | 0.785 | 0.433 |
| Lymphocyte (×10⁹/L)    | 2.09±0.746       | 2.06±0.733           | 0.44  | 0.660 |
| Hemoglobin (g/L)       | 122.88±20.366    | 126.35±20.867        | -1.628| 0.104 |
| Prealbumin (g/L)       | 263.23±67.392    | 273.96±69.317        | -1.518| 0.130 |
| Albumin (g/L)          | 39.53±6.472      | 39.53±7.098          | 0.028 | 0.978 |
| C-reactive protein (mg/L)| 6.06±3.396      | 6.67±3.237           | -1.791| 0.074 |
| Creatinine (umol/L)    | 101.84±33.194    | 99.40±33.274         | 0.712 | 0.477 |
| Urea nitrogen (mmol/L) | 5.57±1.700       | 5.32±1.695           | 1.424 | 0.155 |
| Triglyceride (mmol/L)  | 1.30±0.667       | 1.29±0.673           | -0.549| 0.583 |
| Fasting blood-glucose (mmol/L)| 6.22±1.370 | 6.09±1.385           | 0.854 | 0.394 |
| LDL-C (mmol/L)         | 3.70±1.418       | 3.64±1.333           | 0.432 | 0.666 |
| IgA (g/L)              | 2.19±0.958       | 2.32±0.980           | -1.221| 0.223 |
| IgG (g/L)              | 11.82±3.559      | 12.07±3.340          | -0.695| 0.488 |
| IgM (g/L)              | 1.70±0.648       | 1.75±0.597           | -0.868| 0.386 |
| CD3+ cell (/ul)        | 1800.33±625.165  | 1737.70±608.106      | 0.987 | 0.324 |
| CD4+ cell (/ul)        | 1063.71±883.960  | 883.96±272.177       | 6.692 | <0.001|
| CD8+ cell (/ul)        | 643.36±263.817   | 723.14±286.999       | -2.788| 0.006 |
| NK cell (10⁹/L)        | 0.40±0.225       | 0.36±0.195           | 1.565 | 0.118 |
| B cell (10⁹/L)         | 0.26±0.120       | 0.30±0.143           | -2.725| 0.007 |
| ADL                    | 75.77±11.603     | 79.84±11.382         | -3.439| 0.001 |
| GDS                    | 3.42±1.707       | 2.96±1.409           | -2.585*| 0.010 |
| MNA                    | 21.80±4.627      | 23.11±4.207          | -2.904| 0.004 |
| PG-SGA                 | 0.02±0.186       | 1.97±0.810           | -0.415*| 0.678 |

* Non-parametric test was adopted with t-statistics; CI – cognitive impairment; BMI – Body Mass Index; TSF – triceps skin fold; LDL-C – low density lipoprotein cholesterol; IgA – immunoglobulin A; IgG – immunoglobulin G; IgM – immunoglobulin M; NK cell – natural killer cell; B cell – bursa dependent lymphocyte; ADL – activities of daily living; GDS – global deterioration scale; MNA – mini nutritional assessment; PG-SGA – patient-generated subjective global assessment.
However, no differences were found in the following parameters: height, weight, body mass index (BMI); systolic pressure, diastolic pressure; pulse pressure; waistline; biceps circumference; TSF; number of leukocytes, lymphocytes, blood platelets; hemoglobin; prealbumin; albumin; CRP; creatinine; urea nitrogen; cholesterol; triglyceride; LDL-C; fasting blood-glucose; IgA; IgG; IgM; number of CD3+ cells; number of NK cells; or PS-SGA score (all \(P > 0.05\)).

**Table 3.** Comparison of MMSE score between the CI group and the normal group in elderly patients with chronic diseases.

|                  | CI group | Normal group | \(t\)  | \(P\)   |
|------------------|----------|--------------|--------|---------|
| Total score      | 25.970±1.455 | 28.510±1.100 | -18.738 | <0.001  |
| Directive force  | 7.057±1.641  | 8.581±1.105  | -10.272 | <0.001  |
| Immediate memory | 2.990±0.078  | 2.990±0.095  | 0.316   | 0.752   |
| Calculating ability | 4.910±0.281 | 4.970±0.175  | -2.178  | 0.030   |
| Delayed memory   | 2.560±0.497  | 3.000±0.067  | -10.992 | <0.001  |
| Naming           | 1.990±0.078  | 2.000±0.067  | -0.219  | 0.827   |
| Retelling        | 0.990±0.078  | 0.990±0.095  | 0.316   | 0.752   |
| Reading comprehension | 3.670±0.072 | 3.990±0.095  | -9.07   | <0.001  |
| Writing          | 0.784±0.910  | 1.000±0.000  | -8.918  | <0.001  |
| Visual-spatial ability | 0.784±0.910 | 1.000±0.000  | -8.918  | <0.001  |

CI – cognitive impairment; MMSE – Mini-mental State Examination.

**Table 4.** Comparison of MoCA score between the CI group and the normal group in elderly patients with chronic diseases.

|                  | CI group (n=163) | Normal group (n=222) | \(t\)  | \(P\)   |
|------------------|------------------|----------------------|--------|---------|
| Total score      | 22.910±1.784     | 27.970±1.368         | -30.290 | <0.001  |
| Visual-spatial ability and execution ability | 4.500±0.502 | 4.550±0.498 | -0.989 | 0.323   |
| Naming           | 2.990±0.078      | 2.990±0.095          | 0.316  | 0.758   |
| Attention and calculation | 2.450±1.928 | 5.810±0.396 | -21.901 | <0.001  |
| Language         | 2.550±0.499      | 2.990±0.116          | -11.045 | <0.001  |
| Abstract thinking ability | 1.990±0.078 | 1.980±0.133 | 1.095  | 0.274   |
| Delayed memory   | 4.500±0.502      | 5.000±0.067          | -12.454 | <0.001  |
| Directive force  | 3.920±1.540      | 4.660±1.093          | -5.225 | <0.001  |

CI – cognitive impairment; MoCA – Montreal cognitive assessment scale.

MoCA scores in the CI group and normal group in elderly patients with chronic diseases

A comparison of MoCA scores between the CI group and normal group can be seen in Table 4, showing significant differences between the 2 groups in total score, attention, calculating ability, language, delayed memory, and directive force (all \(P<0.05\)), but no significant differences in visual-spatial ability, execution ability, naming, and abstract thinking ability (\(P>0.05\)).

Logistic regression analysis for risk factors of CI in elderly patients with chronic diseases

The influential factors for CI were screened from Tables 1 and 2, with CI as the dependent variable. The multiple logistic regression analysis included: number of B cells, cerebral infarction history, number of CD4+ cells, admission times, GDS score, age, MNA score, and number of CD8+ cells. The results revealed...
Table 5. Logistic regression analysis for risk factors of CI in elderly patients with chronic diseases.

| Independent variable | B    | S.E.  | Wald  | P     | Exp (B) | Exp (B) 95% C.I. |
|----------------------|------|-------|-------|-------|---------|------------------|
| CD4+ cell            | 0.343| 0.078 | 19.141| <0.001| 1.409   | 1.209–1.643      |
| CD8+ cell            | -0.001| 0.000 | 7.136 | <0.001| 0.999   | 0.998–1.000      |
| B cell               | -2.561| 1.027 | 6.222 | 0.013 | 0.077   | 0.010–0.578      |
| GDS                  | 0.248| 0.085 | 8.578 | 0.003 | 1.282   | 1.086–1.514      |
| ADL                  | -0.042| 0.012 | 13.072| <0.001| 0.959   | 0.937–0.981      |
| MNA                  | -0.068| 0.031 | 4.930 | 0.026 | 0.934   | 0.880–0.992      |
| Diabetes             | -0.129| 0.265 | 0.236 | 0.626 | 0.879   | 0.522–1.478      |
| Cerebral infarction  | 1.004| 0.271 | 13.721| <0.001| 2.73    | 1.605–4.646      |
| Hearing loss         | 0.089| 0.263 | 0.115 | 0.735 | 1.093   | 0.886–1.380      |
| Eyesight diminution  | 0.304| 0.270 | 1.268 | 0.260 | 1.355   | 0.799–2.298      |
| Age                  | 0.169| 0.030 | 31.063| <0.001| 1.185   | 1.116–1.257      |
| Education level      | 0.273| 0.265 | 1.060 | 0.303 | 1.314   | 0.781–2.209      |
| Admission times      | 0.343| 0.078 | 19.141| <0.001| 1.409   | 1.209–1.643      |

CI – cognitive impairment; B cell – bursa dependent lymphocyte; GDS – Global Deterioration Scale; ADL – activities of daily living; MNA – Mini Nutritional Assessment; B – regression coefficient; S.E. – standard error; 95% CI – 95% confidence interval.

Discussion

CI is a common psychiatric problem among the elderly, exerting a severely negative influence on quality of life and increasing mortality [19,20]. Therefore, the present study aimed to investigate the risk factors for CI in elderly patients with chronic diseases.

At present, the diagnosis of CI in elderly patients mainly depends on clinical evaluation [21]. Therefore, the present study was based on clinical feasibility. HAMD-24 was used to exclude patients whose psychological factors may affect the evaluation of cognitive function, and CDR was used to exclude those who could not independently participate in the subsequent evaluation. Then, participants were initially screened using the clinically widely-used MMSE to avoid the ceiling effect, and those regarded as cognitively normal after initial screening was evaluated again. Finally, 163 cases were included in the CI group for the subsequent research. Since most of participants in the study had similar educational backgrounds, no difference was found in several items of MMSE between the normal group and the CI group. In addition, recent research assessed these indices [18,22], with chronic diseases history, immunologic function, and nutritional status emphasized. In the present study, the specific items were chosen based on clinical practice. For instance, education background was assessed according to years in school instead of only the degree awarded; and when chronic diseases were chosen to be included in the study, the spectrum of disease of actually hospitalized patients was given priority. Patients with visual and hearing difficulties, which had no effects on the evaluation results, were included to minimize the selection bias.

The capacity to perform many cognitive processes deteriorates with age and can be determined by neuro-psychological measurements, and it is in fact a normal physiological process and must be distinguished from pathological syndromes [23]. Our study found that age and education level of the elderly patients with chronic diseases were 2 major factors influencing cognitive function, which was confirmed by Gross et al. [24] and Mi et al. [25]. In addition to age as an independent influential factor of CI and education level as a protective factor of cognitive function, sex is also widely seen as an influential factor of CI and education level as a protective factor of cognitive function.
factor in CI [26], which, however, showed no difference between the 2 groups in the present study. The reason may be that the participants had higher education background in general and a relatively small number of women were involved in this study. The 2 groups showed significant differences in ADL and GDS scores in univariate analysis, and ADL and GDS scores were obviously associated with CI in logistic regression analysis. However, the mechanism underlying the association is uncertain.

In terms of information on social behavior, quality of life improves if spouses are alive and patients are well cared for, with no smoking and no drinking, but none of these factors showed an obvious difference between the normal group and the CI group. Poor sleep quality was not only one of the symptoms of CI, but was also an influential factor on the evaluation of cognitive function [27]. Against conventional wisdom, a high-meat diet appeared to be a protective factor for cognitive function in our study. Reviewing the investigation process, we found that most participants were used to eating high-protein lean meat instead of high-fat and high-calorie food, which needs to be confirmed with further exploration of diet. Patients in the CI group showed more admission times, which may be because they indeed needed treatment due to diseases or due to poor neuropsychological test results caused by the mental and physical stress of long-term treatment.

For nutrition, MNA score was positively correlated with cognitive function according to the results of univariate analysis and logistic regression analysis, which was in accordance with the previous study [18]. However, the cause-and-effect relationship between nutritional factors and cognitive function remain unclear. For PG-SGA, no difference was found between the 2 groups, perhaps because the elderly patients failed to make a correct self-evaluation of their weight and disease status or they misunderstood the items on the PG-SGA scale.

For measurable clinical indices, there was no difference between the two 2 groups in several routine examination items, but the 2 groups differed from each other in immunologic function, which is an increasingly studied aspect of cognitive function [22]. Regarding the effects caused by the above-mentioned factors, patients in the CI group exhibited more CD4+ cells but fewer CD8+ and B cells, which provides a promising research direction based on the animal experiment [28], which is the influence of immunologic function on improvement of cognitive function.

Patients with chronic diseases such as heart failure were at a 2-fold increased risk of impaired cognitive function compared with healthy individuals of same age in the domains of psychomotor speed, memory, attention, and executive function [29]. It is clinically significant to discuss common diseases and cognitive function for the purpose of control and prevention of chronic diseases. The most common diseases were included in the present study, among which type 2 diabetes mellitus, multifocal cerebral infarction, hearing ability, and eyesight exhibited significant differences between the 2 groups, and these diseases were proved to be valuable predictors after logistic regression analysis. Type 2 diabetes mellitus and multifocal cerebral infarction may induce CI through vascular injury [30,31]. Although participants with hearing and vision loss were always diagnosed as CI by mistake when taking scale tests, we still found that difficulties in hearing and seeing led to cognitive decline because they failed to have enough cognitive resource capacity for tasks or they were isolated from society [32,33]. Importantly, other studies have indicated that hypertension, hyperuricemia, and hypercholesterolemia may be associated with cognitive functions [34–36], but this was not found in the present study, perhaps due to the differences in methodology, intervention, course of diseases, and comorbidities. Methods currently used to prevent cognitive decline in elderly people with chronic diseases are pharmacological interventions, physical exercises, and cognitive training using mental exercises [37]. After training, there are moderate benefits in language, self-rated anxiety, and functional ability, and moderate improvements in episodic memory, semantic memory, executive functioning, working memory, and visual-spatial ability, as well as in attention processing speed, MMSE, self-rated memory problems, quality of life, activities of daily life, and self-rated depression [38].

**Conclusions**

To sum up, the present study indicates that cerebral infarction history, number of CD4+ cells, admission times, GDS score, and age are risk factors of CI in elderly patients with chronic diseases; therefore, these factors may serve as clinical prevention targets. However, there are still several limitations to the present study that provide direction for future research. Firstly, elderly patients with CI could be further divided into different types, including vascular, mixed, and degenerated CI, or those with CI could also be further divided on the basis of research objective. Secondly, the relationship between the courses of diseases as well as comorbidities and cognitive function requires further improvement. Finally, the influence of pharmacological intervention on cognitive function of patients with chronic diseases is expected to be researched in depth. Therefore, further research is needed to extend our knowledge beyond this work.

**Conflicts of interest**

None.
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