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ORIGINAL ARTICLE

Comorbidity Burden of Dementia: A Hospital-Based Retrospective Study from 2003 to 2012 in Seven Cities in China

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Abstract Dementia is increasing dramatically and imposes a huge burden on society. To date, there is a lack of data on the health status of patients with dementia in China. In an attempt to investigate the comorbidity burden of dementia patients in China at the national level, we enrolled 2,938 patients with Alzheimer's disease (AD), vascular dementia (VaD), or other types of dementia, who were admitted to tertiary hospitals in seven regions of China from January 2003 to December 2012. The Charlson Comorbidity Index (CCI) was used to evaluate the comorbidity burden of the patients with dementia. Among these patients, 53.4% had AD, 26.3% had VaD, and 20.3% had other types of dementia. The CCI was 3.0 ± 1.9 for all patients, 3.4 ± 1.8 for those with VaD, and 3.0 ± 2.1 for those with AD. The CCI increased with age in all patients, and the length of hospital stay and daily expenses rose with age and CCI. Males had a higher CCI and a longer stay than females. Moreover, patients admitted in the last 5 years of the study had a higher CCI than those admitted in the first 5 years. We found that the comorbidity burden of patients with dementia is heavy. These findings provide a better understanding of the overall health status of dementia patients, and help to increase the awareness of clinicians and policy-makers to improve medical care for patients.

Keywords Alzheimer's disease · Vascular dementia · Prevalence · Comorbidity · Charlson comorbidity index

Introduction

With advancing age, an increasing number of elderly people suffer from dementia, the most common neurodegenerative syndrome, which causes deterioration in memory and other cognitive functions [1]. Dementia causes great harm to patients, and it also adds a substantial

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financial burden to society. China, the world's most populous country, is facing population aging: the number of people aged over 60 accounts for 13.3% of the total population [2, 3]. Dementia is increasingly becoming a major health challenge, with an estimated 7 to 9 million dementia patients in China [4]. Most of these patients have Alzheimer's disease (AD), followed by vascular dementia (VaD), and other subtypes of dementia [5]. It has been reported that most dementia patients suffer from other comorbidities, such as diabetes, hypertension, chronic pulmonary disease, heart disease, and inflammatory disease [6–8]. To date, the general health status and disease burden of patients with dementia in China remain largely unknown. Therefore, we conducted this study to investigate the general health condition and comorbidity burden of patients with different subtypes of dementia in seven cities in different regions of China.

Methods

Participants

To investigate the comorbidity burden of patients with dementia, we conducted a hospital-based, retrospective survey in seven regions across China: Chongqing (southwest), Chengdu (southwest), Guangzhou (southeast), Fuzhou (southeast), Lanzhou (northwest), Wuhan (central), and Shenyang (northeast) One large-scale hospital in each city was chosen. The criteria for enrollment eligibility of a hospital were as follows: (1) were accessible to every patient in the city, (2) had a Neurology Department for specialist-based clinical diagnosis of dementia, (3) had an established computerized system for medical records since 2003, and (4) were willing to participate in the study.

All participants enrolled had been hospitalized between January 1, 2003 and December 31, 2012 and diagnosed with AD, VaD, or other forms of dementia, including mixed dementia, frontotemporal dementia, Lewy body dementia, Parkinson's disease with dementia, alcoholic dementia, hydrocephalus dementia, posttraumatic dementia, or unclassified dementia. Patients admitted to the hospitals were given a medical examination, including clinical laboratory, electrocardiogram, X-ray, and computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. Dementia and its types were diagnosed by experienced neurologists based on the medical examination and neuropsychological assessment, according to the international diagnostic criteria, such as the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association [9], and the National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l'Enseignement en Neurosciences [10]. All participants included in this study were > 45 years old, diagnosed with AD, VaD, or other dementia, and spent > 24 h in hospital. Patients were excluded for the following reasons: (1) indefinite diagnosis; (2) total hospital stay > 3 months; (3) died in hospital; or (4) incomplete medical information. Inpatients without dementia from the same hospital were enrolled in the control group. The same number of age- and sex-matched controls were included. This study was approved by the Institutional Review Boards of Daping Hospital, Third Military Medical University. Obtaining informed consent from participants was waived by the Board due to the retrospective nature of the study, as per the Ethical Review of Biomedical Research Involving Human Beings issued by National Health and Family Planning Commission of China. All methods were in accordance with the approved guidelines and regulations.

Data Extraction

All demographic and clinical data—name, gender, age, hospital registration number, admission/discharge date, visit times, hospitalization expenses, and comorbidities such as hypertension, dementia, depression, diabetes mellitus, cancer, and other diseases included in the Charlson Comorbidity Index (CCI) [11, 12]—were extracted from the hospitals' databases, which used clinical codes from the 9th or 10th International Classification of Diseases (ICD-9 or ICD-10). The extracted data were imported into EpiData software (version 3.1). Multiple hospitalizations were identified by the patient's name, age, gender, and registration number. The length of stay was the discharge date minus the admission date, and the daily hospitalization expense (cost per day) was calculated by dividing the total cost by the length of stay. For patients who were hospitalized more than once in a calendar year, all diagnoses were pooled. For patients who were hospitalized multiple times in different calendar years, the data were analyzed separately by calendar year.

Comorbidity Burden Calculation

No standard approach for the measurement of multimorbidity exists. Current indexes for measuring multimorbidity are mainly based on individual severity or influence on other outcomes, such as mortality, hospital stays, or quality of life. Although there is no "gold standard" for measuring multimorbidity, numerous relative indexes are widely used. The most frequently applied is CCI which reflects both the number and severity of comorbidities from which one patient suffers. We analyzed the morbidities from four

aspects: the number of disorders, CCI, length of hospital stay, and daily hospitalization expenses.

Statistical Analysis

All values are the means and standard deviations for continuous variables, and percentages for categorical variables. Differences in demographic characteristics and comorbidities among groups were assessed using analysis of variance (ANOVA) and χ^2 tests, where appropriate. One-way ANOVA trend tests were used to investigate the differences in length of hospital stay, daily hospitalization expenses, and CCI between each group. Multivariate ANOVA was used to investigate the differences of CCI between two periods adjusted for age and gender. Propensity score matching was used to match age and gender in AD and VaD patients using Stata (version 11.0) [13, 14]. Two-sided P values < 0.05 were defined as statistically significant. All analyses were performed with SPSS (version 18.0, SPSS Inc., Chicago, IL).

Results

Characteristics of Participants

We compared the comorbidity burden of dementia patients with age- and gender-matched cognitively normal controls who were admitted to hospital at the same time. Dementia patients had more disorders and a higher CCI than non-dementia patients (Table S1), indicating that the comorbidity burden of patients with dementia is heavier than non-dementia patients.

As shown in Table 1, 53.4% of the dementia patients had AD, while 26.3% had VaD, and 20.3% had other types of dementia. The mean age of the AD patients was higher than the VaD patients (77.6 ± 9.8 *vs* 72.8 ± 10.1, $P < 0.01$). All types of dementia had higher frequencies in males than females, and VaD was more common than AD in males (66.1% *vs* 60.3%, $P < 0.01$). The number of disorders in all patients was 2.6 ± 1.8, and AD patients had more disorders than VaD patients (2.8 ± 1.7 *vs* 2.7 ± 1.6, $P < 0.01$). The CCI of all patients was 3.0 ± 1.9, and that for VaD patients was higher than for AD patients (3.0 ± 2.1 *vs* 3.4 ± 1.8, $P < 0.01$) (Table 1).

Stroke, hypertension, and diabetes were the three most common comorbidities in dementia patients. Compared with VaD patients, AD patients frequently had chronic pulmonary disease, cancer, congestive heart failure, psychoses, and depression, while less frequently having stroke, hypertension, diabetes, coronary artery disease, and hemiplegia or paralysis (Table 1). In stratified analyses by age and gender, there was no significant difference between the AD and VaD groups in the frequencies of coronary artery disease, chronic pulmonary disease, cancer, congestive heart failure, psychoses, and depression (Tables S2 and S3).

The number of admissions due to dementia has increased year-on-year from 2003 to 2012 (Fig. S1). The number of patients with AD, VaD, and other forms of dementia from each city are shown in Table S4. Among the individual diseases indexed in the CCI, cerebrovascular disease, diabetes mellitus, chronic pulmonary disease, hemiplegia, and myocardial infarction were the most frequent, ranking from most to least common in AD patients. Meanwhile, in VaD patients, the diseases indexed in the CCI were cerebrovascular disease, diabetes, hemiplegia, myocardial infarction, and chronic pulmonary disease, in rank order (Table S5).

Comorbidity Burden and Age

To investigate the association between comorbidity burden and age, all participants were divided into six groups according to age (< 65, 65–69, 70–74, 75–79, 80–84, and ≥ 85 years). Using one-way ANOVA trend tests, we found that the CCI increased with age in patients with AD ($F = 81.003$, $P < 0.01$), VaD ($F = 29.496$, $P < 0.01$), and other types of dementia ($F = 57.131$, $P < 0.01$) (Fig. S2). Then we further compared the comorbidities of patients with young-onset and late-onset dementia. Those with late-onset dementia had a higher CCI than those with young-onset dementia (3.2 ± 2.0 *vs* 2.3 ± 1.5, $P < 0.01$) (Table S6). Stroke (52.7% *vs* 36.0%, $P < 0.01$), hypertension (52.3% *vs* 28.8%, $P < 0.01$), diabetes (25.1% *vs* 14.4%, $P < 0.01$), coronary artery disease (23.3% *vs* 2.9%, $P < 0.01$), and chronic pulmonary disease (13.3% *vs* 3.1%, $P < 0.01$) were more frequent in patients with late-onset dementia.

Comorbidity Burden and Gender

To eliminate the influence of age on comorbidity burden, we compared the burden in males and females at the same age. Among all patients, males had a higher CCI than females in all age groups < 65 and > 80 years. In AD patients, males tended to have a higher CCI than females, but only in the older age groups (80–84 and ≥ 85 years) (Table 2). This finding was statistically significant. In VaD patients, this tendency also occurred, but no significant differences in CCI between males and females were found. In addition, we found that the male and female VaD patients had higher CCIs than the corresponding groups of AD patients at several ages. Among all dementia patients, hypertension, stroke, coronary artery disease, diabetes, and chronic pulmonary disease were the most common comorbidities in males, while females more frequently had the

Table 1 Demographic characteristics and comorbidities of patients with different subtypes of dementia

	Overall	AD	VaD	Other Dementia	*P* value[a]
Cases, *n* (%)	2938 (100)	1570 (53.4)	772 (26.3)	596 (20.3)	
Age (years, mean ± SD)	75.0 ± 11.1	77.6 ± 9.8	72.8 ± 10.1	71.1 ± 13.4	< 0.01
Male gender, *n* (%)	1861 (63.3)	947 (60.3)	510 (66.1)	404 (67.8)	< 0.01
Number of disorders (mean ± SD)	2.6 ± 1.8	2.8 ± 1.7	2.7 ± 1.6	2.0 ± 1.6	< 0.01[b]
CCI (mean ± SD)	3.0 ± 1.9	3.0 ± 2.1	3.4 ± 1.8	2.5 ± 1.5	< 0.01[b]
Comorbidities, *n* (%)					
Stroke	1468 (50.0)	682 (43.4)	548 (71.1)	238 (39.9)	< 0.01
Hypertension	1423 (48.4)	670 (42.7)	496 (64.2)	257 (43.1)	< 0.01
Diabetes	686 (23.3)	353 (22.5)	233 (30.2)	100 (16.8)	< 0.01
Coronary artery disease	585 (19.9)	322 (20.5)	128 (16.6)	135 (22.7)	0.02
Chronic pulmonary disease	341 (11.6)	234 (14.9)	65 (8.4)	42 (7.0)	< 0.01
Hemiplegia or paralysis	250 (8.5)	109 (6.9)	113 (14.6)	28 (4.7)	< 0.01
Cancer	189 (6.4)	134 (8.5)	33 (4.3)	22 (3.7)	< 0.01
Congestive heart failure	187 (6.4)	119 (7.6)	38 (4.9)	30 (5.0)	0.02
Psychoses	167 (5.7)	112 (7.1)	26 (3.4)	29 (4.9)	< 0.01
Depression	102 (3.5)	77 (4.9)	13 (1.7)	12 (2.0)	< 0.01

[a]AD *vs* VaD

[b]Adjusted for age and gender

comorbidities stroke, hypertension, diabetes, coronary artery disease, and myocardial infarction (Table S7).

Changes in Comorbidity Burden During the Study Period

Based on admission year, all participants were divided into two groups: those admitted in the first 5 years (2003–2007) and those in the last 5 years (2008–2012). Patients admitted in the last 5 years had higher CCIs than those admitted in the first 5 years in the AD group (3.6 ± 2.4 *vs* 3.3 ± 2.3, $P < 0.01$), the VaD group (3.9 ± 2.0 *vs* 3.3 ± 1.5, $P < 0.01$), and in all patients with dementia (3.1 ± 1.4 *vs* 2.9 ± 1.4, $P < 0.01$) (Table 3).

Length of Hospital Stay and Daily Expenses

To investigate the association among the length of stay and daily hospitalization expenses with comorbidity burden, the CCI was categorized into five grades (0 to 1, 2, 3, 4, and ≥ 5). The length of stay and daily expenses both increased with age (Table 4) and CCI (Fig. S3) in all patients. Moreover, males had longer hospital stays than females > 70 years old, while the daily expenses did not significantly differ between groups (Table 4). No differences were found in length of stay and daily expenses between AD and VaD patients (Tables S8 and S9).

Discussion

By studying a large cohort of 2938 hospitalized dementia patients in seven hospitals in different regions in China from 2003 to 2012, we found that VaD patients had a heavier disease burden than those with AD or other dementias. In this study, significant positive correlations of CCI with age were found in each type of dementia, and the CCI was higher in VaD than in AD patients. The CCI also tended to be higher in males than in females, and it increased significantly over the ten years of the study. In addition, the length of hospital stay and daily hospitalization expenses increased with age and CCI, and tended to be higher in males than in females.

The number of inpatients with dementia has increased over the years, indicating that more patients have access to appropriate treatment. This may have resulted from improvements in quality of life and awareness of medical conditions; alternatively, it might also indicate that more elderly people are suffering from dementia as Chinese society ages. Consistent with previous studies [15], the mean age of AD patients was significantly higher than those with other types of dementia, supporting the idea that age is the main risk factor for AD. Interestingly, we found that VaD patients had a higher CCI after matching for age and gender, indicating that they suffer a larger number of more severe comorbidities than other subtypes of dementia. It was expected that CCI increased with age in our cohort.

Table 2 Comparison of CCI among patients with different dementia types stratified by age and gender

Age	Total			AD			VaD			Other dementia		
	M	*F*	*P* value	M	*F*	*P* value	M	*F*	*P* value	M	*F*	*P* value
< 65	2.4 ± 1.6 (275)	1.9 ± 1.5 (212)	0.01	1.9 ± 1.5 (81)	1.9 ± 1.1 (92)	0.86	3.3 ± 1.7 (97)[a]	3.2 ± 1.6 (50)[b]	0.68	1.9 ± 1.3 (97)	1.5 ± 0.7 (70)	< 0.01
65–69	2.6 ± 1.6 (170)	2.6 ± 1.4 (123)	0.87	2.7 ± 2.1 (63)	2.3 ± 1.3 (57)	0.19	2.8 ± 1.3 (65)	3.1 ± 1.3 (45)[b]	0.25	2.2 ± 1.4 (42)	2.4 ± 1.7 (21)	0.73
70–74	3.1 ± 1.7 (266)	2.9 ± 1.7 (190)	0.21	3.0 ± 2.0 (107)	2.8 ± 1.9 (101)	0.58	3.4 ± 1.6 (99)	3.1 ± 1.6 (55)	0.22	2.8 ± 1.4 (60)	2.7 ± 1.5 (34)	0.92
75–79	3.1 ± 1.8 (388)	3.1 ± 1.8 (233)	0.84	3.1 ± 2.1 (211)	3.1 ± 2.0 (146)	0.76	3.4 ± 1.7 (104)	3.3 ± 1.5 (60)	0.87	2.5 ± 1.2 (73)	2.3 ± 0.8 (27)	0.46
80–84	3.7 ± 2.3 (375)	3.0 ± 1.8 (170)	< 0.01	3.7 ± 2.4 (218)	3.0 ± 1.8 (113)	< 0.01	4.0 ± 2.1 (90)	3.8 ± 1.8 (31)[b]	0.67	3.3 ± 2.1 (67)	2.2 ± 1.3 (26)	0.01
85+	3.7 ± 2.2 (387)	2.9 ± 1.7 (149)	< 0.01	3.6 ± 2.3 (267)	2.8 ± 1.7 (114)	< 0.01	4.4 ± 2.6 (55)[a]	3.5 ± 1.6 (21)	0.14	3.3 ± 1.6 (65)	2.6 ± 1.7 (14)	0.11
Total	3.2 ± 2.0 (1861)	2.7 ± 1.7 (1077)	< 0.01	3.2 ± 2.2 (947)	2.7 ± 1.8 (623)	< 0.01	3.5 ± 1.9 (510)[a]	3.3 ± 1.5 (262)[b]	0.08	2.6 ± 1.6 (404)	2.1 ± 1.3 (192)	< 0.01

Data shown as mean ± SD (*n*)

[a] $P < 0.05$, male AD *vs* male VaD patients; [b] $P < 0.05$, female AD *vs* female VaD patients

It is well known, particularly in the elderly, that organs gradually decline with age and their physiological functioning continues to decline with increasing age. Therefore, as dementia patients age, the comorbidity burden they are likely to suffer increases, with higher financial burden on their families and society.

It is also well known that females are more likely to be diagnosed with AD [16]. However, there were more male than female patients with AD or VaD in our study; this is not consistent with findings from a recent study which showed that females have a higher prevalence of dementia, including AD and VaD, than males in the general population in China [5]. Several reasons could account for this difference. First, males may be hospitalized at higher rates than females in China. Males may have more opportunities to receive medical care as they are thought to be the "backbone" of a family and have a better socioeconomic status than females in China. Second, we found that males tended to have a higher CCI than females, possibly because the prevalence of common diseases in males is more frequent than in females [17]. Consequently, males were more likely to be admitted to hospital, and had longer stays than females in our study. Consistent with a previous study that suggested that disease spectra differ between males and females in the general population [18], our study also revealed different comorbidities between male and female dementia patients, as reflected by higher prevalence of hypertension, coronary artery disease, chronic pulmonary disease, hemiplegia, and renal disease in males than in females.

We also found that participants admitted in the last 5 years of the study had a higher CCI than those admitted in the first 5 years. It has been reported that the comorbidity burden has continuously increased despite continuous increases in global life expectancy over the past 40 years [19]. However, the improvements in health concerns and diagnostic levels could also partially explain the increased comorbidity burden in recent years in China.

As VaD is most frequently caused by cerebrovascular disease, our findings that VaD patients had higher frequencies of stroke and hemiplegia are to be expected. Among all dementia patients with a mean age of 75 years, 48.8% were diagnosed with hypertension. A previous study conducted in a sample representative of the general Chinese population showed that > 65% of the elderly suffer from hypertension [20], which is markedly higher than in this study. After matching for age and gender, the prevalence of hypertension in AD patients was 39.1% and in VaD patients was 64.1%. The prevalence of hypertension in VaD was significantly higher than that in AD, in accordance with previous studies showing that the association between hypertension and dementia is stronger for VaD than AD [21].

Table 3 Comparison of CCI in patients admitted during 2003–2007 and 2008–2012

Type	CCI (mean ± SD)		
	2003–2007	2008–2012	*P* value
AD	3.3 ± 2.3	3.6 ± 2.4	< 0.01
VaD	3.3 ± 1.5	3.9 ± 2.0	< 0.01
Other dementia	2.6 ± 1.8	2.7 ± 1.6	0.69
Overall	2.9 ± 1.4	3.1 ± 1.4	< 0.01

Recently, a study conducted on a representative sample of the Chinese general population showed that the overall prevalence of diabetes is 22.5% for people aged 60–69 years and 23.5% for people aged > 70 years [22]. The prevalence of diabetes among United States adults aged 65 years and older is 21.2% [23]. In our dementia samples, the prevalence of diabetes was 23.3%, slightly higher than the broader elderly population in China. Diabetes is a known risk factor for dementia, especially for VaD [24]. The higher prevalence of cerebrovascular disease, hypertension, and diabetes in VaD patients suggests that the association of vascular risk factors with dementia is more robust for VaD than AD.

Numerous epidemiological studies have shown that chronic obstructive pulmonary disease (COPD) increases the risk of developing dementia [25–27]. COPD and AD are thought to share several mechanisms of neuronal damage [28]. Our previous study suggested that COPD is associated with higher plasma levels of amyloid-beta (an AD biomarker) and inflammatory cytokines [29], which are closely associated with AD [7]. In this study, chronic pulmonary disease (mostly COPD) occurred more frequently in AD patients than VaD patients. Taken together, these findings suggest that COPD increases the risk of developing AD.

A total of 6.4% of dementia patients suffered from cancer in this study, which is higher than the 5-year cancer prevalence of 0.56% estimated for East Asia [30]. However, numerous epidemiological studies have reported an inverse association between cancer and AD [31, 32], and people diagnosed with AD may have some biological protection from cancer [33]. The opposite conclusion in this study may be because our sample primarily consisted of elderly people aged > 60 years who were hospital-based, and some patients with cancer were more likely admitted to hospitals. Moreover, VaD patients showed a lower frequency of cancer than AD patients; this is not consistent with previous findings in which cancer has been linked to AD but not VaD [34]. The lower prevalence of cancer in VaD patients is an interesting finding that deserves further investigation.

One strength of our study is the large sample size of patients with dementia from different regions in China during a period of 10 years. The main limitation is that, as a retrospective study, cluster random selection for recruiting hospital or stratified sampling was not applied, and only patients admitted to the hospital were enrolled. These patients would have more severe dementia or comorbidities. This limitation might make selection bias, such as Berkson's bias, unavoidable. In addition, inter-rater agreement could not be evaluated in this retrospective study. Therefore, the results should be interpreted as a measure of the comorbidities and hospital burden in patients with dementia rather than as the actual incidence or prevalence rates in general patients with dementia. Furthermore, due to the nature of this study, a sex- and age-matched control from the general population was not enrolled, making it difficult to provide a fair picture of the comorbidity burden in general patients with dementia. Another limitation is that the exact subtype of dementia is difficult to accurately diagnose without biomarkers which were not applicable at the time, although we selected tertiary hospitals that had better accuracy in disease diagnosis.

In conclusion, for the first time, we have investigated the disease burden of a large cohort of Chinese dementia patients at the nationwide level, giving a better

Table 4 Comparison of the length of hospital stay and daily expenses of all patients stratified by age and gender

Age	Length of stay (days, mean ± SD)				Daily hospitalization expenses (relative value, mean ± SD)			
	Overall*	M	*F*	*P* value	Overall*	M	*F*	*P* value
< 65	11.3 ± 7.1	11.5 ± 7.2	11.0 ± 7.0	0.53	Ref	1.0 ± 0.6	1.0 ± 0.7	0.69
65–69	12.9 ± 8.4	13.2 ± 7.7	12.6 ± 9.3	0.64	1.1 ± 0.6	1.0 ± 0.6	1.1 ± 0.6	0.20
70–74	14.7 ± 12.3	17.5 ± 14.2	11.3 ± 8.5	< 0.01	1.1 ± 0.6	1.0 ± 0.6	1.2 ± 0.7	0.16
75–79	15.7 ± 12.2	17.1 ± 13.1	13.6 ± 10.2	< 0.01	1.1 ± 0.6	1.1 ± 0.6	1.0 ± 0.6	0.10
80–84	18.1 ± 15.1	19.3 ± 15.6	16.0 ± 13.8	0.09	1.2 ± 0.6	1.2 ± 0.6	1.1 ± 0.5	0.11
85+	21.1 ± 15.1	22.8 ± 15.7	18.0 ± 13.5	0.03	1.2 ± 0.7	1.1 ± 0.6	1.3 ± 0.7	0.13
Overall	15.6 ± 12.5	17.1 ± 13.5	13.4 ± 10.5	< 0.01	1.1 ± 0.6	1.1 ± 0.6	1.1 ± 0.6	0.95

*$P < 0.01$. One-way ANOVA trend test was used to investigate the correlations between length of stay, daily expenses, and age

understanding of the overall health status of dementia patients and providing a useful reference for future comparative studies. The findings of this study could help to increase the awareness of clinicians and policy-makers about the detection of frequently occurring comorbidities in AD or VaD patients and improve overall medical care and the quality of life of patients. In addition, it has recently been suggested that systemic disorders are associated with Aβ metabolism in the brain and AD pathogenesis [35]. Given the heavy burden of comorbidities in both AD and VaD, management of dysfunction of the peripheral tissues and organs is necessary to effectively treat AD and other types of dementia in the future.

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Compliance with Ethical Standards

Conflict of interests The authors declare no financial or other conflicts of interests.

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