Title

Cause of Death Determined by Full-body Autopsy in Neuropathologically Diagnosed Dementias

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Cause of death determined by full-body autopsy in neuropathologically diagnosed dementias – The Biobank for Aging Studies of the University of Sao Paulo (BAS-USP), Brazil

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Abstract

OBJECTIVE: This study aims to compare causes of death in the most prevalent neuropathologically diagnosed dementias.

METHODS: We analyzed causes of death in a community-based cohort of participants aged 50 or older, submitted to full-body autopsy and a comprehensive neuropathological examination of the brain. Individuals with Alzheimer's disease (AD), vascular dementia (VaD), mixed dementia (AD+VaD), or dementia with Lewy bodies (DLB) were compared with individuals with no dementia.

RESULTS: In a sample of 920 individuals, 456 had no dementia, 147 had AD, 120 had VaD, 53 had DLB, and 37 had AD+VaD. Pneumonia as the cause of death was more frequent in the AD (p=0.023), AD+VaD (p=0.046), and DLB (p=0.043) groups. In addition, VaD (p=0.041) and AD+VaD (p=0.028) groups had a higher frequency of atherosclerosis as detected by full-body autopsy.

CONCLUSION: Our findings highlight the importance of preventive measures regarding atherosclerosis and pneumonia in patients with dementia. Moreover, due to cognitive impairment, these patients may not fully account for symptoms to make early detection and diagnosis possible. These results confirm findings from previous studies that were based on clinical data, with added accuracy provided by neuropathological diagnosis and full-body autopsy reports.

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5. Conflicts of interest

The authors declare no conflict of interest.

Keywords

neuropathological diagnosis; causes of death; mortality; autopsy; Alzheimer's disease

1. Introduction

Alzheimer's disease (AD), vascular dementia (VaD), dementia with Lewy bodies (DLB) are the most common causes of dementia[1,2]. AD is responsible for 60% of dementia cases[3] and is associated with higher mortality[4]. VaD is also associated with significant loss of life expectancy, as well as DLB [5,6]. In a study involving clinically diagnosed AD, conditions such as pneumonia, dehydration, and decubitus ulcers were more frequent in the death certificates of individuals with AD than in those of individuals with no dementia[7].

VaD, the second most common type of dementia, is associated with cardiovascular risk factors, such as diabetes, smoking, coronary disease, hypertension, high levels of cholesterol, and obesity[8]. Different cerebrovascular pathologies such as large infarcts, multiple microinfarcts, strategic infarcts (e.g., thalamus, hippocampus), cerebral hypoperfusion, or cerebral hemorrhages, may cause VaD. Cerebrovascular changes can often coexist with AD pathologies in a condition referred to as mixed dementia[9]. In studies based on clinical diagnosis, individuals with VaD had more cardiovascular mortality and cerebrovascular disease than individuals with AD[10,11].

DLB is the third leading cause of dementia. Unlike AD, DLB is more common among men and often occurs at a younger age[12]. The survival time after diagnosis is usually shorter than that of individuals with AD[13] or with Parkinson's Disease and no dementia[14,15]. Respiratory causes of death (CoD) were reported to be more common in individuals with DLB than in individuals with AD[11].

Few studies compared different CoD among dementia types based on full-body autopsy reports and neuropathological assessments; these studies were carried out with smaller cohorts and convenience samples from hospitalized patients[16,17]. In a study conducted in Denmark with 308 individuals, those with AD died more often from pneumonia than those with no dementia. CoD of individuals with other types of dementia did not differ from CoD of those with no dementia[17]. The other study, conducted in Switzerland with 342 individuals, found that cardiovascular CoD were more frequent in VaD than in AD[16].

Therefore, the present study aims to compare CoD according to full-body autopsy reports among different types of dementia confirmed by neuropathological examination in a large multiethnic, community-based sample. We hypothesize that dementias can be associated with different disorders which may be risk factors for and complications of these dementias. Therefore, a better understanding of conditions associated with dementias might help in preventive strategies and early treatment of its complications.

2. Methods

2.1. Participants

Participants of this study were deceased individuals submitted to autopsy at the Sao Paulo Autopsy Service of the University of Sao Paulo (SVOC-USP). They were part of the Biobank for Aging Studies of the University of Sao Paulo (BAS-USP). In Sao Paulo city, an autopsy is mandatory when the non-traumatic CoD is unclear due to lack of medical assistance or insufficient information before death. Subjects were included during weekdays after the next kin agreed to participate in the study and donate the brain. Briefly, after consenting, trained gerontologists applied the clinical and functional assessments about the deceased to the next of kin. Further information regarding methodological procedures of the BAS-USP can be reached elsewhere[18]. Inclusion criteria for the BAS-USP were participants aged 50 years and older with a knowledgeable informant who had had at least weekly contact with the deceased to provide clinical information. Exclusion criteria for the BAS-USP were: (i) brain tissue unsuitable for neuropathological analyses (e.g., cerebrospinal fluid pH < 6.5, or significant acute brain lesions, such as hemorrhages or tumors); and (ii) inconsistent clinical data provided by the informant. All BAS-USP protocols, the informed consent form, and procedures follow international and Brazilian regulations for research involving humans and were approved by the local and federal research committees.

2.2. Neuropathological evaluation

Brain tissue was obtained within 24 hours of death. One hemisphere of the brain was fixed in paraformaldehyde, and the other was frozen at −80°C. After fixation, samples from 13 regions were selected and embedded in paraffin (middle frontal gyrus, middle, and superior temporal gyri, angular gyrus, superior frontal, and anterior cingulate gyrus, visual cortex, hippocampal formation at the level of the lateral geniculate body, amygdala, basal ganglia at the level of the anterior commissure, thalamus, midbrain, pons, medulla oblongata, and cerebellum). The paraffin blocks were cut into 5 μm thick sections and stained with hematoxylin and eosin. Immunohistochemistry with antibodies against β-amyloid, phosphorylated tau, TDP-43, and a-synuclein was used in selected sections.

AD was diagnosed according to the Consortium Establish a Registry for Alzheimer's disease (CERAD) criteria for neuritic plaques[19] and the Braak and Braak score for neurofibrillary tangles[20].

The macrovascular assessment included both hemispheres, cerebellum, and brain stem. Microvascular changes were analyzed semi-quantitatively using H&E staining in all sampled structures. Diffuse small-vessel disease (SVD) in the white matter, hippocampal sclerosis, and lacunae, microinfarcts, and infarcts were registered. Cerebral amyloid angiopathy (CAA) was verified using anti-β amyloid immunostaining. The diagnosis of VaD was made in cases with one large chronic infarct (>1 cm) or three lacunae in strategic areas (thalamus, frontocingular cortex, basal forebrain, and caudate, medial temporal area, and angular gyrus)[21]. SVD was diagnosed when there was widespread and at least moderately severe SVD in three cortical regions. SVD included small-vessel arteriosclerosis/atherosclerosis, arteriolosclerosis, and lipohyalinosis[22]. CAA was not included in the SVD group. Cases

were classified as positive for CAA when CAA was diffusely in the parenchyma of at least three different cortical areas. In this study, SVD and pure CAA were not considered sufficient for the diagnosis of VaD because the literature remains unclear regarding vascular dementia diagnosis in cases with no apparent parenchymal lesions[23]. Individuals that presented three or more infarcts in these areas were diagnosed with VaD[22].

Lewy bodies disease was classified using the Braak staging for Parkinson's disease (Lewy body disease), and Braak Parkinson's disease stage ≥ 3 was considered for positive diagnosis[24].

2.3. Full-body autopsy reports

The CoD was identified by full-body autopsies performed by a pathologist and classified according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

First, in the full-body autopsy, an external inspection of the body is performed. After that, the internal examination of the cranial cavity and thoracic and abdominal cavities is accomplished. Next, the pathologist measures the volume of fluids and blood, exams integrity and limits of the anatomy (external appearance of the organs and their location), detects adhesions and obliteration of the cavities, lesions, and hemorrhages - the general principles of pathological anatomy. Samples of abnormal areas of organs such as the kidney, spleen, lung, liver, heart, and brain are collected for anatomopathological analysis. A brief report regarding how the death occurred and preexisting diseases is also collected with a close family member to confront macro and microscopic findings[25].

In our analysis, we have considered the CoD reported in the full-body autopsy carried out by a pathologist. As death can be a multifactorial event, all national full-body autopsy reports are filled in according to a hierarchical chain of events that led to a person's death, CoD being the last event. Therefore, we have also analyzed the official CoD combined with three other causes related to death (CrD) presented in the autopsy report of each individual.

The ICD-10 diagnoses reported in the full-body autopsy were evaluated. The most frequent group categories were cardiovascular diseases and their subgroups ischemic heart diseases (atherosclerosis restricted to the coronary arteries), pulmonary embolism, hypertension-related diseases, pericarditis, systemic atherosclerosis; pneumonia; chronic obstructive pulmonary disease; digestive system diseases; diabetes; cancer; anemia; urinary tract infection; and chronic and acute renal disease.

Information regarding age, sex (as gender identity was not available), and ethnicity (Caucasian or non-Caucasian) were collected from the full-body autopsy reports. Ethnicity was reported by the informant and included various ethnic backgrounds. For example, Caucasians included people of European descent, and non-Caucasians included people of African descent and indigenous people.

2.4. Clinical assessment

Following the BAS-USP procedure, a trained nursing staff applied protocols to an informant who had close contact with the deceased (at least once a week for the last six months before death) to obtain clinical information of the deceased. The Clinical Dementia Rating scale (CDR) – informant interview was applied to retrospectively evaluate cognitive and functional performance[26].

2.5. Dementia groups

We divided participants into six groups: (1) AD; (2) VaD; (3) DLB; (4) mixed dementia (AD+VaD); (5) other types of dementia; (6) without dementia. The group of other types of dementia was very heterogeneous and included mixed dementias composed of different combinations, such as AD, VaD, and DLB; AD and DLB; VaD and DLB; incidental progressive supranuclear palsy; VaD and dementia with a predominance of fibrillar tangles; AD and multiple system atrophy, among others. Therefore, the group of other types of dementia was excluded from the analysis.

2.6. Statistical analysis

For the statistical analysis, Chi-square test was used to compare categorical variables among the five neuropathological dementia groups (AD, VaD, AD+VaD, DLB, and no dementia), and ANOVA was used for quantitative variables. Differences in the CoD and CrD were obtained by logistic regression. Different CoD and CrD were considered the dependent variable. They were classified as present or absent in each logistic regression, the group with no neuropathological diagnosis was considered the reference category, and it was compared with each of the dementia groups. Sex, age, and ethnicity were used as covariates. All CoD and CrD presented in the full-body autopsy reports were assessed, except for uncommon diseases ($n \leq 65$). Uncommon diseases were excluded since there were usually less than five occurrences in each dementia group, limiting the power to the logistic regression analyses. Logistic regression was also used to analyze the association of CDR 2 and 3 (later stages of dementia) with the CrD pneumonia. We used Stata 15 for statistical analyses, and the alpha level was set at the 5% level.

3. Results

Our sample consisted of 920 individuals in which 456 participants had no dementia, 147 had pure AD, 120 had pure VaD, 53 had pure DLB, 37 had AD+VaD, and 107 had other types of dementia. The group other types of dementia were excluded from this analysis.

The remaining sample consisted of 813 individuals, of which 413 (50.8%) were female, the mean age was 73.8±11.4 years old, the mean schooling was 3.9±3.7 years, and 620 (76.3%) were Caucasian (Table 1). When comparing the dementia groups, we found differences regarding gender ($p<0.001$), age ($p<0.001$), and ethnicity (Caucasian and non-Caucasian, $p=0.040$). After post hoc analysis using the no dementia group as the reference category, women had a greater prevalence of AD ($p<0.001$) and AD+VaD ($p=0.025$). Individuals in all dementia groups were older than individuals without dementia ($p<0.001$ for all) and had lower schooling ($p<0.001$ for all), except for the AD+VaD group ($p=0.999$).

Regarding ethnicity, after post hoc analysis using the group of individuals without dementia as a reference category, no difference was found (AD p=0.407, VaD p=0.576, AD+VaD p=357, DLB p=0.339).

The most frequent CoD and CrD are presented in Table 2.

When we examined the CoD, pneumonia was more frequent in the AD+VaD (OR=2.72, 95% CI=1.14–6.53, p=0.024) and DLB (OR=2.42, 95% CI=1.13–5.12, p=0.023) groups; cardiovascular diseases were less frequent in the AD (OR=0.64, 95% CI=0.41–0.97, p=0.035) group (Table 3). No differences among dementia groups were found in CoD classified as cardiovascular diseases, ischemic heart diseases, hypertension-related diseases, and pulmonary embolism.

When we examined the CrD, systemic atherosclerosis was more frequent in the VaD (OR=1.57; 95% CI: 1.02–2.38, p=0.041) and AD+VaD groups (OR=2.24; 95% CI: 1.10–4.58, p=0.028). Pneumonia was more frequent in participants with AD (OR=1.99; 95% CI: 1.10–3.58, p=0.023), AD+VaD (OR=2.51; 95% CI: 1.02–6.19, p=0.046) and DLB (OR=2.25; 95%CI: 1.03–4.93, p=0.043). (Table 4). Later stages of dementia (CDR 2 and 3) were significant for pneumonia CrD (p=0.012). No differences among dementia groups were found in CrD classified as cardiovascular diseases, ischemic heart diseases, hypertension-related diseases, diabetes, pulmonary embolism, and cancer.

4. Discussion

In a community-based sample of 813 individuals, we compared CoD and CrD in different neuropathologically confirmed dementias. One finding was greater frequency of pneumonia as the CoD and CrD in individuals with AD+VaD and in individuals with DLB; pneumonia was also more frequent as CrD in individuals with AD. Furthermore, later stages of dementia were significant for pneumonia CrD in all dementia groups. Another finding was that systemic atherosclerosis was more frequent among CrD in individuals with VaD or AD+VaD.

Our study combined the high level of accuracy of dementia diagnoses from neuropathological evaluations with data from full-body autopsy reports in a community-based sample. There are only two similar studies based on complete autopsy reports and on neuropathological examination in the literature; both used data from convenience samples involving hospitalized patients[16,17]. In accordance with our study findings, Attems et al.[17] found, in a sample of 308 individuals, that those with AD (n=135) died more frequently from pneumonia when compared to non-demented individuals and died less from cardiovascular diseases. Differently from our study, Kammoun et al.[16] found that, in a sample of 342 individuals, pneumonia, cardiovascular, and cerebrovascular CoD were more frequent in VaD when compared to AD or AD+VaD. However, they did not find differences between the CoD of demented and non-demented individuals[16]. One possible explanation for these divergences is the difference in sample origin (community versus hospital) and sample size.

Other studies also found higher frequencies of pneumonia as the CoD in neuropathologically diagnosed AD such as a retrospective observational study of 204 patients admitted to a hospital that underwent post-mortem examination[27].

Regarding VaD and mixed dementia, a small study with 38 individuals also found a higher proportion of atherosclerosis in VaD. However, they only compared individuals with AD with VaD[28].

There are studies with larger samples based on death certificates with full-body autopsy reports and clinical diagnosis of the dementias[10,11]. One of the studies was based on a sample of 5,368 individuals with dementia, but it lacked a control group[11]. Using AD as a reference to compare the CoD with other dementia groups, similarly to our study, they found that those with VaD died more frequently from cardiovascular causes. Again, similarly to our study, they also found that individuals with DLB had higher mortality due to respiratory causes. The other study was based on a sample of 2,924 individuals, had a control group, and categorized dementia in AD, VaD, and other/mixed dementia[10]. Pneumonia was more frequent as CoD in individuals with dementia when compared to non-demented individuals. They also found that VaD individuals died more often from cerebrovascular diseases. Unlike our study, another critical study based on death certificates and clinical diagnosis of AD, with a sample of 27,948 individuals with AD and a matched comparison cohort without dementia, found that AD participants were more likely to die from a nervous system disease than individuals without AD and that the most common CoD were nervous system, circulatory system, and neoplasms[29]. Methodological differences and greater sample size may explain the variance in the results.

A meta-analysis including studies based on death certificates, clinical diagnosis of dementia, studies with necropsies and neuropathological evaluations, and studies with mixed methodologies also confirmed that pneumonia was the CoD more frequently associated among individuals with dementia[30]. They also found that in hospitalized patients, the prevalence of pneumonia as the CoD was higher in both demented and non-demented individuals and that individuals with dementia continued to die more from pneumonia than non-demented individuals. Among possible explanations for pneumonia being a frequent CoD in individuals with dementia are dysphagia and aspiration, immobility, poor nutritional status, and decreased immune response[31]. Interestingly, a recent meta-analysis found that in studies based on full-body autopsy information, 50% of individuals with dementia had pneumonia as the CoD. In studies based on death certificates that considered clinical information, this frequency was only 20%[32], probably due to underreported or under-diagnosed pneumonia. Indeed, the concordance between the CoD reported by autopsy reports and death certificates was only 52% in one study[33]. Also, a meta-analysis found a discrepancy rate of 30% to 63% for the CoD when comparing clinical information and full-body autopsies[34]. Therefore, a full-body autopsy probably yields more reliable statistics of CrD[33,35].

Our findings emphazises the importance of primary prevention and treatment of atherosclerosis and pneumonia in dementia patients. For example, pneumonia in patients may be prevented by decreasing the risk of aspiration and improving mobility and

nutrition status. Besides, pneumonia is a major CrD in individuals with AD, AD+VaD, and DLB probably because older adults with dementia may not present classic symptoms of pneumonia or other lower respiratory infections, contributing to its being underdiagnosed, as shown previously.

Our study should be comprehended considering its limitations. Currently, the neuropathological criterion for VaD diagnosis is not accepted universally[36,37]. We used a criterion with high specificity for VaD, but that could underestimate the diagnosis of VaD in our sample[38]. Another potential limitation is that we classified amyloid plaques as diffuse or neuritic based on morphological features seen on β-amyloid immunohistochemistry. In contrast, neurofibrillary tangles are classified based on morphological features on phospho-tau immunohistochemistry and were not verified by silver or thioflavin-S staining. Finally, we did not adjust statistical analyses by apolipoprotein E (APOE) ε4 status since we did not have APOE measurements for the whole sample.

Our study was based on a community sample that included older adults (and not only very old participants) and came from a multiracial country such as Brazil add valuable data to the literature. It is important to note that most of the neuropathological studies have been conducted in American and European countries, in individuals with high levels of education, and predominantly white. As far as we know, this is the study with the largest sample that combined reliable information of the full-body autopsy reports and neuropathological assessment to diagnose dementias. As stated already several studies indicate that death certificates (based on clinical diagnoses) are less accurate than full-body autopsy reports[33–35].

In summary, our study confirms that individuals with AD, AD+VaD, and DLB died more frequently from pneumonia, and individuals with VaD and AD+VaD presented more systemic atherosclerosis compared to individuals with no dementia. Thus, our findings are consistent with those of previous clinical studies but provide more accurate information because our study included full-body autopsy reports and neuropathological evaluations of individuals from a multiethnic, community-based sample.

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Table 1:

Demographic characteristics according to dementia groups (n=813).

	AD n=147 (18.1%)	**VaD n=120 (14.8%)**	**AD+VaD n=37 (4.5%)**	**DLB n=53 (6.5%)**	**No dementia n=456 (56.1%)**	**p†**
Female, n (%)	95 (64.6%)	67 (55.8%)	25 (67.6%)	23 (43.4%)	203 (44.5%)	**<0.001**
Age (years) ± mean (SD)	80.4 ± 8.1	76.4 ± 9.7	84.0 ± 7.3	78.2 ± 7.8	69.6 ± 11.5	**<0.001**
Schooling (years) ± mean (SD)	2.8 ± 2.9	2.2 ± 2.9	4.0 ± 4.8	3.1 ± 2.2	4.5 ± 4.0	**<0.001**
Caucasian, n (%)	119 (81.0%)	83 (69.2%)	32 (86.5%)	45 (84.9%)	341 (74.8%)	**0.040**

*Data are presented as means and standard deviation (SD), and for categorical values as the number of cases (n) and its percentage (%).

†Chi-square test.

‡Note: AD: Alzheimer's Disease, VaD: Vascular Dementia, DLB: Dementia with Lewy Bodies, AD+VaD: mixed dementia.

Table 2:

The causes related to death and causes of death were classified according to the ICD-10 and are presented below in descending order.

Disease	ICD-10	CoD – n (%)	CrD – n (%)
Cardiovascular diseases	I	569 (69.4%)	641 (78.8%)
Ischemic heart diseases	I20, I21, I22, I23, I24, I25	288 (35.4%)	355 (43.7%)
Pulmonary embolism	I26, I27	83 (10.2%)	84 (10.3%)
Hypertension-related diseases	I10, I11, I12	66 (8.1%)	187 (23%)
Pericarditis	I30, I31	47 (5.8%)	48 (6%)
Systemic atherosclerosis	I70	3 (0.3%)	319 (39.3%)
Pneumonia	J06, J18, J20, J69, J85	100 (12.3%)	105 (12.9%)
Chronic obstructive pulmonary related disease	J42, J43, J44	11 (1.3%)	35 (4%)
Digestive system diseases	K	38 (4.7%)	65 (8%)
Diabetes	E14	0	97 (11.9%)
Cancer	C	16 (2.0%)	69 (8.5%)
Anemia	D50, D53, D57, D64, D68	14 (1.7%)	14 (1.7%)
Urinary tract infection	N10, N11, N30, N39	3 (0.3%)	7 (1.9%)
Chronic and acute renal disease	N03, N08, N12, N15, N18, N25, N35	0	5 (0.6%)

*Number of cases (n) and its percentage (%)

†Notes: ICD-10: International Statistical Classification of Diseases and Related Health Problems 2010, CrD: Causes related to Death, CoD: Causes of Death

Table 3:

Association between immediate cause of death (CoD) and dementia groups (n=813)

	AD		VaD		AD+VaD		DLB	
	OR (95% CI)	P*	OR (95% CI)	P*	OR (95% CI)	P*	OR (95% CI)	P*
Cardiovascular diseases	0.63 (0.41–0.97)	**0.035**	0.874 (0.55–1.38)	0.565	0.90 (0.42–2.00)	0.796	0.70 (0.38–1.30)	0.261
Ischemic heart diseases	1.03 (0.67–1.59)	0.884	1.22 (0.79–1.90)	0.367	1.47 (0.71–3.05)	0.302	0.70 (0.36–1.36)	0.286
Pulmonary embolism	0.81 (0.43–1.51)	0.508	0.89 (0.44–1.77)	0.728	0.39 (0.12–1.38)	0.143	0.59 (0.20–1.75)	0.340
Hypertension-related diseases	0.61 (0.27–1.37)	0.232	0.66 (0.29–1.50)	0.324	0.85 (0.24–3.07)	0.804	1.87 (0.80–4.38)	0.152
Pneumonia	1.71 (0.94–3.10)	0.080	1.60 (0.85–3.01)	0.149	2.42 (1.13–5.20)	**0.024**	2.42 (1.13–5.19)	**0.023**

*Logistic regression models adjusted for age, schooling, gender, ethnicity; reference category was the no dementia group

†Note: AD: Alzheimer's Disease, VaD: Vascular Dementia, DLB: Dementia with Lewy Bodies, AD+VaD: mixed dementia, OR: Odds Ratio, 95% CI: 95% Confidence Interval.

Table 4:

Association between causes related to death (CrD) and dementia groups (n=813)

	AD		VaD		AD+VaD		DLB	
	OR (95% CI)	**P***	**OR (95% CI)**	**P***	**OR (95% CI)**	**P***	**OR (95% CI)**	**P***
Cardiovascular diseases	0.69 (0.42–1.14)	0.127	1.00 (0.58–1.70)	0.984	0.81 (0.34–1.90)	0.621	0.54 (0.28–1.04)	0.066
Ischemic heart diseases	1.03 (0.67–1.59)	0.884	1.22 (0.79–1.90)	0.367	1.47 (0.71–3.05)	0.302	0.70 (0.36–1.36)	0.286
Pulmonary embolism	0.81 (0.43–1.51)	0.508	0.89 (0.44–1.77)	0.728	0.39 (0.12–1.38)	0.143	0.59 (0.20–1.75)	0.340
Hypertension-related diseases	0.61 (0.27–1.37)	0.232	0.66 (0.29–1.50)	0.324	0.85 (0.24–3.07)	0.804	1.87 (0.80–4.38)	0.152
Systemic Atherosclerosis	1.06 (0.70–1.60)	0.794	1.57 (1.02–2.38)	**0.041**	2.24 (1.10–4.58)	**0.028**	0.60 (0.32–1.15)	0.123
Pneumonia	1.99 (1.10–3.58)	**0.023**	1.53 (0.81–2.93)	0.193	2.51 (1.02–6.19)	**0.046**	2.25 (1.03–4.93)	**0.043**
Diabetes	1.01 (0.54–1.87)	0.981	1.19 (0.64–2.22)	0.575	1.95 (0.72–4.77)	0.143	0.31 (0.07–1.36)	0.114
Cancer	1.07 (0.53–2.13)	0.860	0.60 (0.25–1.40)	0.236	-	-	1.44 (0.60–3.50)	0.417

*Logistic regression models adjusted for age, schooling, gender, ethnicity; reference category was the no dementia group

†Note: AD: Alzheimer's Disease, VaD: Vascular Dementia, DLB: Dementia with Lewy Bodies, AD+VaD: mixed dementia, OR: Odds Ratio, 95% CI: 95% Confidence Interval.