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ORIGINAL ARTICLE

Influence of pneumonia complications on the prognosis of patients with autopsy-confirmed Alzheimer's disease, dementia with Lewy bodies, and vascular dementia

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Abstract

Background: Pneumonia is a major, complicated disease in patients with dementia. However, the influence of pneumonia on the prognosis of patients with varying types of dementia has not been fully evaluated.

Methods: We retrospectively analyzed the data from medical and autopsy reports. All study patients had been hospitalized and underwent brain autopsy in a hospital in Toyohashi, Japan, between 2005 and 2014. The patients with subtypes of dementia, specifically Alzheimer's disease (AD), dementia with Lewy bodies (DLB), or vascular dementia (VaD), were neuropathologically diagnosed and examined. Pneumonia incidence, cause of death, and the clinical time-course of dementia were compared among the dementia subtypes. The time to death from dementia onset (survival time) was compared by the Kaplan–Meier method among subtypes of dementia with or without pneumonia. Risk factors for survival time on all study patients were analyzed with the Cox proportional hazard model.

Results: Of the 157 eligible patients, 63 (40.1%) had AD, 42 (26.8%) had DLB, and 52 (33.1%) had VaD. Pneumonia complication was observed with high incidence in each subtype of dementia, especially in DLB (90.5%). The median total duration from dementia onset to death was 8 years in AD and DLB, and 5 years in VaD. The VaD subtype had more male patients than AD or DLB ($P = 0.010$), and age of death in this group was the youngest among the three groups ($P = 0.018$). A significant difference was observed in the survival time by the Kaplan–Meier method among the three groups ($P < 0.001$) and among the groups with pneumonia ($P = 0.002$). The factors associated with shorter survival time were male gender, pneumonia complications, diabetes mellitus, age of dementia onset ≥ 75 years, and VaD.

Conclusions: Pneumonia complications shortened the survival time of patients with AD, DLB, and VaD.

Keywords: *Alzheimer's disease, dementia with Lewy bodies, dementia, diabetes mellitus, pneumonia, survival time, vascular dementia.*

INTRODUCTION

Dementia has become an illness of major concern among the ageing population globally. Although there is individual variability in the clinical course of dementia, the disease decreases people's life expectancy.[1–4] The primary cause of death in dementia patients is pneumonia, whereas cardiovascular disease and neoplasms are more common in the general population.[4–7] A recent meta-analysis indicated that the odds of pneumonia-associated death were increased in persons with dementia.[8] Although few reports have investigated the association between respiratory function and dementia,[9–11] a current UK study demonstrated an association between forced expiratory volume in 1 s and dementia-related death.[12] We hypothesized that if deterioration in pulmonary function contributes to death in dementia, dementia patients who develop pneumonia will have shorter

lifespans than those without pneumonia. Understanding the influence of pneumonia on clinical time-course of dementia is crucial for predicting the remaining life in patients with dementia and contributes to the development of optimal clinical management of dementia.

Currently, there are three major subtypes of dementia: Alzheimer's disease (AD), dementia with Lewy bodies (DLB), and vascular dementia (VaD). Approximately 90% of the total dementia population in Japan has one of these forms of dementia.[13–15] Previous reports indicated the varied survival time of patients with each dementia subtype.[16–18] Comparisons of survival time between AD and DLB have been inconsistent, with studies showing faster,[19] slower,[20] or no difference.[21–24] The disease progression of AD, DLB, and VaD with and without pneumonia has not previously been elucidated and remains unclear. However, some discrepancies between the clinical and neuropathological diagnoses of each subtype of dementia sometimes make it difficult to interpret the results of such studies.[4–7]

The aims of the present study were to examine the survival time in AD, DLB, and VaD, with and without pneumonia, and to determine the risk factors affecting the time from dementia onset to death.

METHODS

Study design and subjects

The study was conducted at the Choju Medical Institute, Fukushimura Hospital in Toyohashi, Japan, which mainly specializes in psychogeriatrics, neurology, internal medicine, and surgery, and includes a neuropathological research centre.[14] We retrospectively reviewed the charts, medical reports, and autopsy reports, as well as the results of neuropathological examinations, of patients who were hospitalized and deceased between January 2005 and December 2014. All patients had brain autopsies in the neuropathological research centre at the study site. Data were collected in relation to the general and clinical backgrounds of the patients, clinical time-courses, and clinical conditions of patients during the hospitalization, including swallowing dysfunction, nosocomial infections, percutaneous endoscopic gastrostomy, medications, and results of neuropathological examinations.

From the autopsied cases, patients with neuropathological diagnosis of AD, DLB, or VaD by specialized pathologists and neurologists were selected for the study. For cases with both AD and Lewy pathology, low likelihood cases with extensive AD pathology according to the DLB guideline were considered to have AD.[25–27] In addition, cases with both AD and vascular pathology (i.e. mixed dementia) were considered to have AD.

The clinical and general backgrounds, the incidence of pneumonia, underlying and immediate causes of death, and clinical time-courses were compared among the three subtypes of dementia. The risk factors for the time to death from dementia onset (survival time) were analyzed for all eligible patients, as well as between patients with and without pneumonia.

The study was approved by the institutional review boards of the University of Tsukuba and the Choju Medical Institute, Fukushimura Hospital. Written informed consent was obtained from patients' relatives.

Diagnosis and definitions

Two investigators independently reviewed the data and were blinded to the clinical diagnoses written by the physician in charge in order to ensure the dementia subtype and cause of death were accurate. The cause of death, dementia subtype, and other variables were extracted into predesigned data collection forms. We verified the accuracy of the data by comparing the collection forms from each investigator. Any discrepancy was resolved by discussion.

The neuropathological diagnosis of AD, DLB and VaD was assessed with autopsy records and based on published criteria, including the Consortium to Establish a Registry for Alzheimer's Disease,[28–30] Braak scores,[31] and neurofibrillary tangles as described by Mölsä et al.,[32] DLB guidelines,[25–27] and Kosaka's classification.[33,34]

Based on the diagnostic criteria of guidelines for the management of hospital-acquired pneumonia in adults by the Japanese Respiratory Society, the complication of pneumonia may occur either repeatedly or once during hospitalization.[35]

Dementia onset was defined at the time (year) when patients first experienced forgetfulness, disorientation, abnormal behaviour, or delusions according to the Guideline for Dementia 2010.[36] Hospital admission was defined as the time of hospitalization until the patient was discharged.

The immediate cause of death was defined as the final disease, injury, or complication directly causing death. The underlying cause of death was defined as the disease, injury, or corresponding circumstances that initiated the chain of events ultimately leading to death.[5]

Statistical analysis

The data relating to the general and clinical backgrounds of the patients, clinical time-courses including time to death from dementia onset, time to hospital admission from dementia onset, time to death from hospital admission, and causes of death were summarized and compared among groups of each subtype of dementia. The Kruskal–Wallis tests were used for continuous variables, and the χ^2 and Fisher's exact tests were used for categorical variables. Survival curves on the survival times of dementia (years) in groups of patients with AD, DLB, or VaD, with or without pneumonia, were analyzed by the Kaplan–Meier method, and comparisons were made with the log-rank test. To evaluate independent factors for the survival time of dementia, a stepwise method was used for a Cox proportional hazard analysis. Data analyses were conducted using SPSS Statistics 22.0 (IBM, Armonk, NY, USA). For all analyses, significance levels were two-tailed, and $P < 0.05$ was considered significant.

RESULTS

General characteristics of study patients with AD, DLB, and VaD

During the observation period, a total of 261 patients died and were autopsied at Fukushimura Hospital (Fig. 1). Patients who died within 1 week of an emergency visit to the hospital and who did not have data available were excluded from the study; therefore, the study included a total 230 patients. Among them, 157 patients were determined to have AD, DLB, or VaD by neuropathological diagnosis. The numbers of each subtype of dementia were 63 AD (40.1%), 42 DLB (26.8%), and 52 VaD (33.1%).

The general characteristics of the patients with AD, DLB, and VaD are shown in Table 1. While more female patients had AD and DLB, more male patients had VaD. The age of dementia onset among VaD

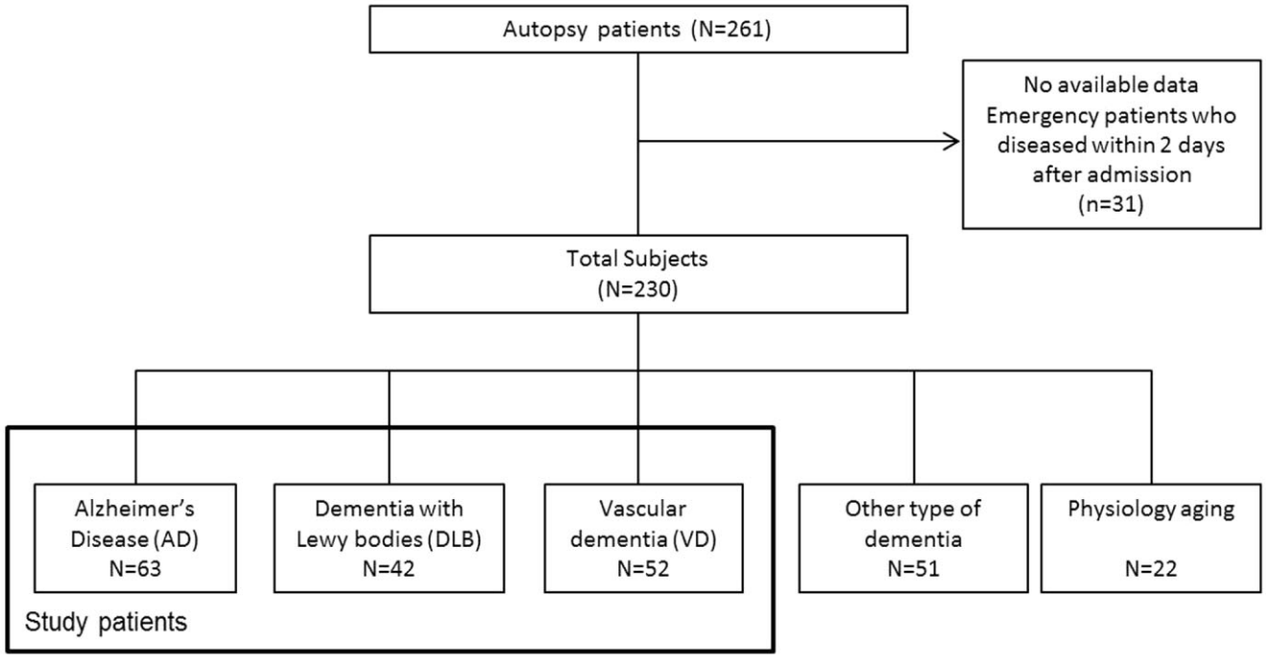

Figure 1 Study population. A total of 261 patients were autopsied at the study site during the observational period. Patients who died within 1 week of an emergency visit to the hospital and who did not have data available were excluded. In total, 157 patients were determined to have Alzheimer's disease, dementia with Lewy bodies, or vascular dementia by neuropathological diagnoses and were eligible for the present study.

Table 1 General characteristics of patients with Alzheimer's disease, dementia with Lewy bodies, or vascular dementia (n = 157)

	AD n = 63	DLB n = 42	VaD n = 52	P-value
Complication of pneumonia, n (%)	56 (88.9)	38 (90.5)	43 (82.7)	0.306†
Gender, n (%)				0.010†
Male	20 (31.7)	12 (28.6)	27 (51.9)	
Female	43 (68.3)	30 (71.4)	25 (48.1)	
Age				
Median age in years of dementia onset (IQR)	79 (72–84)	78 (72–84)	76 (70–82)	0.269§
<65 years, n (%)	8 (12.7)	4 (9.5)	6 (11.5)	0.125†
65–74 years, n (%)	11 (17.5)	9 (21.4)	17 (32.7)	
≥75 years, n (%)	44 (69.8)	29 (69.0)	29 (55.8)	
Clinical characteristics				
Median BMI at admission (IQR) (n = 77)	19 (16–20)	18 (14–21)	19 (18–22)	0.096§
Median weight of brain (IQR) (n = 135)	1047 (980–1170)	1050 (1000–1140)	1080 (982–1153)	0.062§
Pathological findings, n (%)				
Cerebral infarction	27 (42.9)	15 (35.7)	43 (82.7)	<0.001†
Comorbidities, n (%)				
Hypertension	27 (42.9)	11 (26.2)	31 (59.6)	0.001†
Pulmonary emphysema	11 (17.5)	8 (19.0)	10 (19.2)	0.853†
Diabetes mellitus	10 (15.9)	2 (4.8)	14 (26.9)	0.007†
Angina	5 (8.1)	3 (6.5)	3 (6.5)	0.801‡
Heart failure	5 (8.1)	2 (4.3)	2 (3.8)	0.507‡
Malignant neoplasm	10 (16.1)	2 (4.3)	4 (7.7)	0.047†
Events after admission, n (%)				
PEG	19 (30.2)	17 (40.5)	25 (48.1)	0.046†
Urinary tract infection	10 (16.1)	9 (19.6)	8 (15.4)	0.521†
Swallowing dysfunctions	26 (41.3)	23 (54.8)	23 (44.2)	0.157†
Medications, n (%)				
Anti-dementia drug*	12 (19.4)	3 (6.5)	2 (3.8)	0.007†
Benzodiazepines use	6 (9.7)	9 (19.6)	7 (13.5)	0.143†

*Anti-dementia drug included acetylcholine inhibitors and NMDA receptor inhibitor. †χ^2 test. ‡Fisher's exact test. §Kruskal–Wallis test. AD, Alzheimer's disease; BMI, body mass index; DLB, dementia with Lewy bodies; IQR, interquartile range; PEG, percutaneous endoscopic gastrostomy; VaD, vascular dementia.

patients tended to be younger than among AD and DLB patients, but there was no significant difference among the subtypes of dementia. A high incidence of pneumonia complication was seen in all three subtypes of dementia, with no significant difference among the three groups. DLB patients had the highest incidence (90.5%) of pneumonia complication. Cerebral infarction, including asymptomatic condition, was pathologically found in 82.7% of VaD patients, and there was also a high incidence in AD and DLB patients. The major comorbidities were hypertension and diabetes mellitus, especially in patients with VaD.

Causes of death in patients with AD, DLB, and VaD

The underlying and immediate causes of death were examined and compared among the subtypes of dementia (Table 2). Although the causes of death in dementia patients varied, pneumonia was the greatest underlying and immediate cause of death. In 49.2% of AD patients, pneumonia was the underlying cause of death (P = 0.001), and in over 50% of AD and DLB patients, it was the immediate cause of death (P = 0.007); there was significant difference among the subtypes of dementia. More VaD and DLB patients than AD patients had respiratory failure as the immediate cause of death (P = 0.056). Renal failure was the second highest immediate cause of death among VaD patients, with a significant difference among the subtypes (P = 0.046). Sudden death only presented in DLB as an immediate cause of death.

Clinical time-course of dementia in patients with and without pneumonia

The clinical time-courses of dementia patients were compared among the subtypes of dementia and between patients with and without pneumonia (Table 3). Although there was no difference in the age of dementia onset among the three groups, the age of

Table 2 Immediate and underlying cause of death in dementia patients with and without pneumonia (n = 157)

	AD n = 63	DLB n = 42	VaD n = 52	P-value
Underlying cause of death, n (%)				
Pneumonia	31 (49.2)	9 (21.4)	15 (28.8)	0.001†
Cerebrovascular accident	6 (9.7)	3 (7.1)	6 (11.5)	0.405‡
Heart failure	9 (14.5)	13 (28.3)	6 (11.5)	0.006†
Respiratory failure	1 (1.6)	1 (2.2)	2 (3.8)	1.000‡
Renal failure	1 (1.6)	2 (4.3)	5 (9.6)	0.051†
Failure on liver, gallbladder, pancreas	2 (3.2)	2 (4.3)	1 (1.9)	1.000‡
Diabetes mellitus	1 (1.6)	3 (6.5)	0 (0.0)	0.101†
Malignant neoplasm	5 (8.1)	6 (13.0)	6 (11.5)	0.274†
Sepsis	3 (4.8)	3 (6.5)	7 (13.5)	0.061†
Geromarasmus	1 (1.6)	1 (2.2)	0 (1.3)	1.000‡
Sudden unexpected natural death	0 (0.0)	1 (2.2)	0 (0.0)	0.268‡
Seizure	0 (0.0)	0 (0.0)	2 (3.8)	1.000‡
Others	3 (4.8)	2 (4.3)	2 (3.8)	0.967†
Immediate cause of death, n (%)				
Pneumonia	33 (52.4)	22 (52.4)	15 (28.8)	0.007†
Cerebrovascular accident	5 (8.1)	1 (2.2)	4 (7.7)	0.188†
Heart failure	5 (7.9)	1 (2.4)	4 (7.7)	1.000‡
Respiratory failure	2 (3.2)	5 (10.9)	6 (11.5)	0.053†
Renal failure	5 (8.1)	6 (13.0)	11 (21.2)	0.046†
Failure on liver, gallbladder, pancreas	2 (3.2)	0 (0.0)	0 (0.0)	1.000‡
Malignant neoplasm	6 (9.7)	0 (0.0)	4 (7.7)	1.000‡
Sepsis	4 (6.5)	3 (6.5)	6 (11.5)	0.228†
Sudden unexpected natural death	0 (0.0)	3 (7.1)	0 (0.0)	0.610‡
Seizure	1 (1.6)	0 (0.0)	1 (1.9)	1.000‡
Others	4 (6.5)	2 (4.3)	3 (5.8)	0.791†

†χ^2 test. ‡Fisher's exact test. AD, Alzheimer's disease; DLB, dementia with Lewy bodies; VaD, vascular dementia.

Table 3 Clinical time-course of dementia patients with AD, DLB, and VaD (n = 157)

	AD n = 63	DLB n = 42	VaD n = 52	P-value†
Age of dementia onset	79 (72–84)	78 (72–84)	76 (70–82)	0.269
Age of death	86 (82–92)	87 (81–92)	83 (78–87)	0.018
Total years (from onset to death)	8 (5–13)	8 (5–15)	5 (3–9)	0.015
According to pneumonia complication				
With pneumonia (n = 137)	8 (5–13)	8 (5–14)	5 (3–8)	0.006
Without pneumonia (n = 20)	7 (3–12)	13 (5–18)	5 (3–12)	0.181
According to groups of dementia onset age				<0.001
<65 years (n = 17)	17 (13–22)	16 (15–19)	7 (3–11)	
65–74 years (n = 36)	11 (8–13)	12 (8–16)	7 (4–12)	
≥75 years (n = 102)	6 (4–10)	6 (4–10)	5 (3–6)	
Years between dementia onset to admission	6 (2–8)	5 (3–8)	3 (1–6)	0.015
Years between hospital admission to death	2 (1–5)	3 (1–8)	3 (1–5)	0.404

Time-course on each variable is presented as median (interquartile range), years. †Kruskal–Wallis test. AD, Alzheimer's disease; DLB, dementia with Lewy bodies; VaD, vascular dementia.

death of VaD patients was younger than that of AD and DLB patients (P = 0.018). The median survival time for VaD patients was shorter (5 years) than for AD (8 years) and DLB (8 years) patients. Although the number of patients with DLB who did not acquire pneumonia was small, their lifespan was shortened by 5 years if they developed pneumonia (13 vs 8 years). In the analysis on the divided survival time-course, a significant difference was seen between the subtypes of dementia in the time from dementia onset to hospital admission, but no difference was observed in the time from hospital admission to death.

The influence of the complication of pneumonia on clinical time-courses was assessed by the

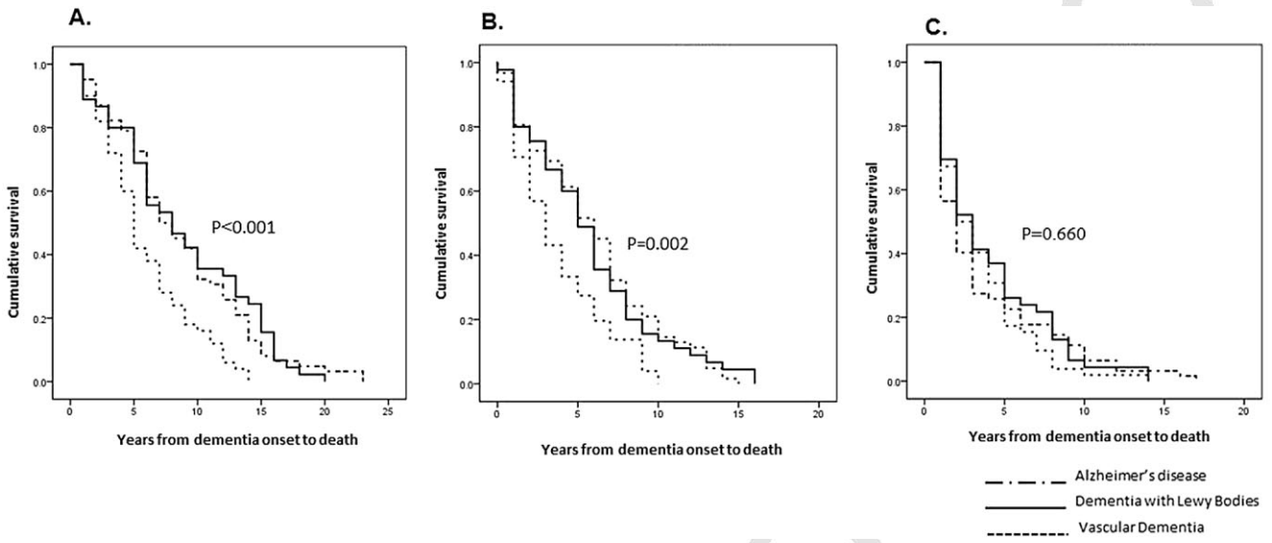

Figure 2 Kaplan–Meier curves on the number of years to death from dementia onset for dementia patients of each subtype: (a) all dementia patients; (b) dementia patients with pneumonia; and (c) dementia patients without pneumonia. There were significant differences among all patients (log-rank test, $P < 0.001$) and patients with pneumonia (log-rank test, $P = 0.002$), but not among patients without pneumonia (log-rank test, $P = 0.660$).

Kaplan–Meier method and compared between the different subtypes of dementia with the log-rank test (Fig. 2). The evaluation of dementia patients ($n = 157$) and dementia patients with pneumonia ($n = 137$) revealed significant differences among the subtypes of dementia ($P < 0.001$ and $P = 0.002$, respectively) (Fig. 2a,b). However, there were no significant differences among the subtypes of dementia in the patients without pneumonia (Fig. 2c).

In the subgroup analysis, the influence of the complication of pneumonia on clinical time-courses was also assessed among different age groups by the Kaplan–Meier method using the log-rank test (Fig. 3). It was observed that the dementia patients aged ≥75 years with pneumonia had shorter survival times than those aged <65 years and 65–74 years with pneumonia. Although the number of patients without pneumonia was small, there was no significant difference among in dementia duration among the different age groups.

Evaluation of risk factors: time to death from dementia onset

Risk factors relating to survival time in dementia patients according to the Cox proportional hazard model

Factors relating to the survival time of dementia were evaluated with the Cox proportional hazard model for dementia patients with and without pneumonia ($n = 157$). The results indicated that the risk factors associated with shorter survival time were male gender, pneumonia, diabetes mellitus, being ≥75 years at the age of dementia onset, and VaD. Being <65 years at onset was associated with longer survival time. The interaction of pneumonia and the dementia subtypes was also examined by this model, but no statistical significance was observed.

DISCUSSION

Using neuropathological diagnoses of dementia, the present study revealed that patients with all three major subtypes of dementia had a high incidence of complications with pneumonia. The median total survival time of dementia onset was 8 years for AD and DLB and 5 years for VaD. Patients with VaD had a shorter survival time than those with AD and DLB. Factors associated with a shorter survival time among dementia patients were male gender, pneumonia complications, diabetes mellitus, being ≥75 years at onset, and VaD.

The World Health Organization has reported that 47.5 million people have dementia and that 7.7 million new cases occur every year.[37] Currently, medications for treating dementia are limited. The development of optimal clinical management strategies for dementia is urgent in order to help patients live a long life.

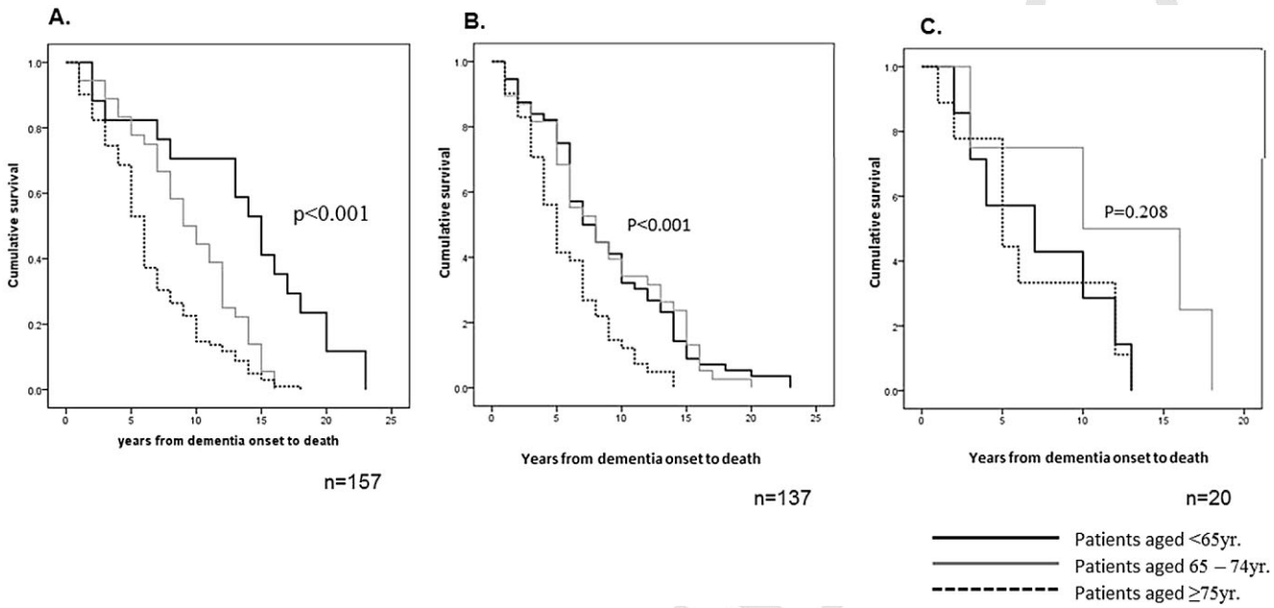

Figure 3 Kaplan–Meier curves on the number of years to death from dementia onset for dementia patients in the age groups <65 years, 65–74 years, and ≥75 years: (a) all dementia patients; (b) dementia patients with pneumonia; and (c) dementia patients without pneumonia. There were significant differences among all patients (log-rank test, $P < 0.001$) and patients with pneumonia (log-rank test, $P < 0.001$), but not among patients without pneumonia (log-rank test, $P = 0.208$). However, there were only a small number of patients without pneumonia.

Pneumonia is the leading cause of death in ageing populations and, in the present study, was the main cause of death of dementia patients, which is consistent with the results of previous autopsy studies.[4,5] Evaluating the effect of pneumonia on the lifespan for dementia patients is also crucial. However, reported survival times vary among dementia patients. The effect of pneumonia on survival time and the differences among dementia subtypes are also unclear.

Previous reports indicated that the mean survival time among DLB patients ranged from 1.8 to 9.5 years.[18] Another study found that the mean survival time after an AD diagnosis ranged from 8 to 12 years.[17] A previous retrospective study on AD found that the median survival from initial diagnosis was 4.2 years for men and 5.7 years for women.[38] In the present study, the median survival time was 8 years for AD and DLB patients and 5 years for VaD patients. One reason for the differences in survival time between AD and DLB may be the accuracy of the clinical diagnosis of dementia. Although differentiation between the clinical diagnosis of dementia and post-mortem diagnosis has been discussed,[39] most previous studies have lacked autopsy confirmation for the specific subtype of dementia. In the present study, the subtypes of dementia were neuropathologically diagnosed and the survival time of dementia evaluated. The results of the present study found that AD and DLB had a similar mean duration (7.1 years) to AD cases in a post-mortem study,[40] but the duration was slightly longer than the 6.1 years found in a meta-analysis of DLB.[18] Another reason for the difference in survival times between this study and previous studies was the definition of initiation of dementia. In our evaluation, disease duration began at the time of disease onset, not from the time of diagnosis. In a previous study, similar results were found between AD and DLB patients when disease duration was examined from disease onset to death, but when duration began at the time of diagnosis, the results significantly differed.[16] When disease duration is examined, an informant (i.e. a friend or family member of the patient) may need to indicate when initial awareness of conditions and symptoms occurred.

Additionally, we compared the survival time of AD and DLB patients with that of VaD patients. Although the aetiopathogenesis of AD, DLB, and VaD are not completely understood, the differences in survival times might be due to the different pathogenesis of each type of dementia. VaD is a progressive disease

that is caused by reduced cerebral blood flow supplying the brain, and it may be associated with some types of cerebral events.[41–43] In the present study, cerebral infarction was a more common comorbidity in VaD than in AD and DLB ($P < 0.001$). Both AD and DLB are neurodegenerative disease, and they may have a slower progression than expansion of cerebral dysfunction of VaD. In addition, VaD involves systemic vascular changes, and it is reasonable to suppose that these changes, in part, contribute to the shortening of survival time. In the present study, cerebral vascular changes were more common in patients with AD than those with DLB; however, there was no difference in survival time between AD and DLB patients, but there was a difference between AD and DLB patients and those with VaD.

Regardless of the subtype of dementia, many dementia patients experienced the complication of pneumonia. One reason was that dementia patients may have weakened defence mechanisms for preventing respiratory tract infections. Previous studies revealed an association between respiratory function and cognition, which is impaired in dementia.[9–11] Once dementia patients have experienced pneumonia, the deterioration of respiratory function may also reduce lifespan. A recent study examining the association between respiratory function and the incidence of pneumonia indicated that for every standard deviation increase in forced expiratory volume in 1 s, the risk of dementia decreased by more than 20%.[12] Our study evaluated the association between pneumonia not only for death but also for survival in patients with dementia. Swallowing dysfunctions are common in patients with dementia and known as a major contributor to the mortality.[44] In this study, among AD, DLB, and VaD patients, the presentation of swallowing dysfunctions in each subtype of dementia did not significantly differ (Table 1). This was not evaluated as an influencing factor on survival time, but the results of this study may indicate that swallowing dysfunction is a risk to mortality and survival time in patients with dementia, regardless dementia subtype. The survival time of patients with DLB and pneumonia was 5 years shorter than that of patients with DLB and no pneumonia, but it should be noted that the number of DLB patients without pneumonia was small. In contrast, similar survival times were observed between AD and VaD patients with and without pneumonia (Table 3). This result suggested that if patients with DLB get pneumonia, the deterioration of respiratory function may be faster than in other subtypes of dementia. This may be because DLB decreased ventilator response to hypercapnia.[45] However, further investigations are needed to clarify this hypothesis.

The Cox proportional hazard model in the present study revealed that male gender, pneumonia complication, comorbidity of diabetes mellitus, being ≥75 years at dementia onset, and VaD were independent risk factors relating to the shortness of survival time in dementia patients. Age <65 years at dementia onset increased survival time (Table 4). Previously, those with type 2 diabetes mellitus were known to have a higher risk of dementia than the general population.[46,47] The present study evaluated diabetes mellitus and found that it is a risk for survival time of dementia patients. The results of the present study suggested the importance of clinical management of repetitive pneumonia and underlying diseases, including diabetes mellitus, during hospitalization of dementia patients, especially patients aged ≥75 years, to expand patients' lifespans.

One limitation of this study was that the time of onset was taken from the medical records and relied on reports from patients, their families, or their caregivers about the commencement of symptoms and signs of dementia. The present study was conducted at an institute specializing in psychogerontology, particularly for patients with dementia. The physicians were specialists with significant clinical experience in consulting with dementia patients. It was thought that time discrepancies with regard to actual onset thought to be no wide range with their report. This

Table 4 Risk factors for time to mortality from dementia onset in dementia patients using Cox proportional hazard model ($n = 157$)

	HR	95%CI	*P*-value
Male gender	1.942	1.362–2.769	<0.001
Pneumonia	1.528	0.935–2.496	0.091
Diabetes mellitus	1.585	1.017–2.470	0.042
Age of dementia onset, <65 years	0.372	0.189–0.734	0.004
Age of dementia onset, ≥75 years	2.266	1.507–3.408	0.000
Vascular dementia	2.041	1.397–2.982	0.000

Baseline adjustment covariates: gender, pneumonia complication, subtypes of dementia (Alzheimer's disease, dementia with Lewy bodies, vascular dementia), groups of onset age (<65 years, 65–74 years, ≥75 years), pneumonia complication, comorbidities (hypertension, diabetes mellitus, heart failure, cerebral infarction, pulmonary emphysema, angina, malignant neoplasm), swallowing dysfunction, urinary tract infection, and percutaneous endoscopic gastrostomy. Presented items of $P < 0.1$.
The interaction of pneumonia and subtypes of dementia was not significant ($P = 0.340$). CI, confidence interval; HR, hazard ratio. *P* value: χ^2 test.

study was conducted at a single medical institution, so further studies are required in other populations before the results can be generalized. We believe this is the first report comparing the survival time of AD, DLB, and VaD patients with and without pneumonia in Japan.

In conclusion, the incidence of pneumonia was high in three different subtypes of dementia and represented an immediate cause of death in patients. Pneumonia complication was a significant factor for disease prognosis in dementia patients. To maximize life expectancy, the prevention of pneumonia and appropriate clinical management of underlying diseases are necessary in dementia patients aged ≥75 years. These results warrant a further prospective cohort study.

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