Pneumonia, Intake Problems, and Survival Among Nursing Home Residents With Variable Stages of Dementia in the Netherlands

Results From a Prospective Observational Study

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Objectives: We explored how pneumonia and intake problems affect survival in nursing home residents in variable stages of dementia.

Methods: In a longitudinal observational study (372 residents) with up to 3.5 years of follow-up, we examined relationships between dementia severity, the development of pneumonia, intake problems, and mortality using joint modeling, Cox models, and mediation analyses. Dementia severity was measured semiannually with the Bedford Alzheimer Nursing Severity-Scale (BANS-S).

Results: The median BANS-S score at baseline was 13 (range, 7 to 28). Pneumonia occurred in 103 (28%) and intake problems in 126 (34%) of 367 residents with complete registration of pneumonia and intake problems. Compared with dementia severity, incident pneumonia and, even more so, incident intake problems were more strongly associated with mortality risk. Pneumonia and intake problems both mediated the relationship between more severe dementia and mortality.

Discussion: Developing pneumonia and intake problems affects survival, and this is not limited to advanced dementia. The occurrence of pneumonia and intake problems are important signals to consider a palliative care approach in nursing home residents with dementia, and an active focus on advance care planning is needed. Future studies should investigate whether this is also relevant for patients in primary care.

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Dementia is an incurable disease and many people will die with or from this disease.[1] In many countries, more than half of people with dementia die in long-term care settings. The majority of these nursing home residents can no longer safely live on their own.[2] Few nursing home residents reach the end stages of dementia with complete ADL impairment, severe verbal and physical impairment, and severe impairment in decision making.[2,3]

During the course of dementia, pneumonia and intake problems frequently occur and may influence quality of life and survival.[4–8] A focus on palliative care goals may be appropriate for nursing home residents with advanced dementia.[1,5,9] However, a palliative goal of care may be also helpful in earlier stages of the disease trajectory,[1] because many nursing home residents die before reaching the stage of advanced dementia.[3,10]

Understanding the clinical course of dementia forms the foundation of physician prognostication and supports advance care planning and palliative care actions.[1,11] However, knowledge about the clinical course of dementia in nursing home residents is limited and is based on findings from retrospective studies, cross-sectional studies, and studies of patients in the advanced stage of dementia.[1,5,12,13] Mitchell et al[5] reported that infections and eating difficulties are hallmarks of advanced dementia, and residents with advanced dementia have a high mortality rate. This is consistent with 3 commonly reported causes of death in nursing home residents with dementia, which are pneumonia, dehydration, and cachexia.[4,8]

Using longitudinal data is important to characterize the disease dynamics, survival, and the role of pneumonia and intake problems as potential mediating factors. This information may help physicians to inform patients and families about the clinical complications to be expected during the course of dementia and support them in establishing care goals, palliative care actions, and advance care planning. To further these goals, we sought to determine the incidence of pneumonia and intake problems and how these health problems affect survival of nursing home residents with dementia. Further, we assessed whether the

severity of dementia is associated with development of pneumonia, intake problems, and with mortality and whether pneumonia and intake problems mediated the relationship between dementia severity and death.

METHODS

Data Collection

We used data from a longitudinal observational study, the Dutch End of Life in Dementia (DEOLD) study.[3] Between 2007 and 2011, we collected prospective and retrospective data on 491 residents in 34 long-term care facilities residing on psychogeriatric wards (almost all dementia).[3] In this article, we only use the data prospectively collected on 372 residents with dementia at any stage who were newly admitted to 28 long-term care facilities and who were enrolled upon admission between January 2007 and July 2009.[3] Elderly care physicians were responsible for data collection by completing written questionnaires.

Individual assessments were performed for up to 3½ years (January 2007 to July 2010) and survival was monitored for an additional year (until summer 2011). A baseline assessment was scheduled 8 weeks after admission, followed by up to a maximum of 5 semiannual assessments. In case of death during the study period, a questionnaire about the last week of life was completed within 2 weeks after death. Physicians additionally registered any incident pneumonia and incident intake problems on a continuous basis. As the median survival time after developing pneumonia and intake problems in our dataset was almost 2 months, we censored survival data in this article at 2 months after having concluded the monitoring of incident pneumonia and intake problems (at 31 August 2010). The study protocol was approved by the Medical Ethics Review Committee of the VU University Medical Center Amsterdam, and written informed consent was obtained from the families.

Measurements

At baseline we measured several resident characteristics. We assessed the place of residence before admission and the 2 most important reasons for admission with prestructured items. Type of dementia was assessed with a prestructured item comprising the categories Alzheimer disease, vascular dementia, Alzheimer disease and vascular dementia, Lewy body/Parkinson disease, and other. The diagnosis of dementia was based on international guidelines.[14–16] We assessed activity of daily living with the Minimum Dataset Set-ADL-Long Form scale,[17,18] ranging from 7 to 28, with higher scores indicating poorer function. We rated residents' illness severity on the Illness Severity Score,[19,20] ranging from 1 to 9; higher scores indicating more severe illness. We assessed nutritional status and 1 hydration status item with prestructured items[21]: (1) cachectic (combining very cachectic and cachectic) or not cachectic (combining normal, adipose, and very adipose); (2) weight loss of $\geq 5\%$ in last month, $\geq 10\%$ in the last 6 months, or no weight loss; and (3) hydration status [not dehydrated (normal), mildly dehydrated, dehydrated, or severely dehydrated].

At baseline and at every semiannual assessment, we assessed dementia stage in 2 ways. To define the severity of dementia on a continuous scale, we used the Bedford Alzheimer Nursing Severity-Scale (BANS-S), with a range of 7 to 28 and higher scores indicating more severe dementia.[22,23] It is suggested that a cutoff score of 17 is appropriate for defining severe (or advanced) dementia, and a score of ≥ 17 is comparable with a Mini-Mental State Examination (MMSE) score under 10.[17,22,23] Physicians (20%, 181/917), or nurses under supervision of the physician (80%, 736/917), assigned the BANS-S scores. In addition, we used the Global Deterioration Scale (GDS)[24] and the Cognitive Performance Scale (CPS)[25] to compare our findings with those of other studies and defined advanced dementia as a GDS score of 7, and a CPS score of 5 or 6. CPS 5 and 6 are associated with mean MMSE scores of 5 and 1.[25]

Physicians continuously registered any incident pneumonia or intake problem, with the date of diagnosis. We collected data about diagnostics, symptoms, and health condition at the time of diagnosis. Pneumonia was judged by the attending physician. To investigate pneumonia severity, we assessed mortality risk with a score specific for patients with pneumonia and dementia, estimating the risk of death within 14 days when treated with antibiotics.[26–28] We defined intake problems as an eating or drinking problem as judged by the attending physician. Physicians assessed the primary reason for the intake problem, with prestructured categories including the option "other reason."

Statistical Analyses

The analyses considered the first episode of pneumonia and the first occurrence of an intake problem. We calculated the length of time from admission until the development of pneumonia or an intake problem, and the survival time afterward, or censored time. Further, we reported the hazard rate of developing pneumonia and of developing intake problems in the first year, and the hazard rate of mortality in the first year.

Table 1 summarizes the stepwise approach in examining the relationships along with the statistical models. First, we assessed the unadjusted direct relationship between dementia severity and mortality (1). The BANS-S that measures dementia severity also includes ADL items (3 out of 7).[29] Second, we separately assessed the relationship between dementia severity and first occurrence of pneumonia (2a), and between dementia severity and first occurrence of intake problems (2b). As the severity of dementia may change over time and therefore may influence the survival time, we used joint modeling. These models jointly analyze longitudinal data and time-to-event data and account for both nonrandom dropout in the longitudinal data and endogenous time-varying covariates.[30] In the first step of the joint model analysis, a linear mixed regression model was used for the longitudinal severity of dementia (BANS-S scores) data. In the second step, we fitted a Cox proportional hazard model to analyze the time to event. In the final step, these 2 models were linked (joined) through their shared random effects. In addition to the joint models, and for reasons of comparability with other studies, we used Cox proportional hazard models with time-dependent covariates to assess the relationships between advanced dementia (yes/no) and, respectively, mortality, pneumonia, and intake problems (1 + , 2a + , and 2b +). Third, to estimate the association between pneumonia and mortality (3a), and between intake problems and mortality (3b), we used 2 Cox proportional hazard models with time-dependent covariates. To assess whether and how dementia severity changed the strength of

TABLE 1. Statistical Analyses Used for the Explored Relationships

Association	Method	Time-dependent Covariates	Dependent Variables	HR (95% CI), *P*; Coefficient, SE
(1) Direct relationship between dementia severity and mortality	Joint model	Dementia severity (BANS-S* at every assessment) Time between assessments of BANS-S* Survival time/censored time	Mortality	**1.19** (1.14-1.23; per point increment), <0.001; 0.172, 0.020
(1 +) Advanced dementia vs. less advanced dementia and mortality	Cox proportional hazard models with time-dependent covariates	Advanced dementia vs. less advanced dementia† Time until advanced dementia Survival time/censored time	Mortality	**1.7** (1.2-2.4), 0.005; 0.51, 0.18
(2a) Direct relationship between dementia severity and first occurrence of a pneumonia	Joint model	Dementia severity (BANS-S* at every assessment) Time between assessments of BANS-S* Time until pneumonia Survival time/censored time	Pneumonia‡	**1.07** (1.01-1.14; per point increment), 0.0220; 0.071, 0.031
(2a +) Advanced dementia vs. less advanced dementia and first occurrence of a pneumonia	Cox proportional hazard models with time-dependent covariates	Advanced dementia vs. less advanced dementia† Time until advanced dementia Time until pneumonia Survival time/censored time	Pneumonia‡	**1.2** (0.7-2.2), 0.57; 0.18, 0.31
(2b) Direct relationship between dementia severity and first occurrence of an intake problem	Joint model	Dementia severity (BANS-S* at every assessment) Time between assessments of BANS-S* Time until intake problem Survival time/censored time	Intake problem‡	**1.16** (1.10-1.23; per point increment), <0.001; 0.152, 0.029
(2b +) Advanced dementia vs. less advanced dementia and first occurrence of an intake problem	Cox proportional hazard models with time-dependent covariates	Advanced dementia vs. less advanced dementia† Time until advanced dementia Time until intake problem Survival time/censored time	Intake problem‡	**1.6** (0.94-2.6), 0.087; 0.44, 0.25
(3a) Direct relationship between pneumonia and mortality	Cox proportional hazard models with time-dependent covariates	Pneumonia‡ (unadjusted) Time until pneumonia Time from pneumonia until survival/censored time	Mortality	**4.1** (3.1-5.4), <0.001; 1.4, 0.148
(3a +) Whether the dementia severity changed the strength of this associations	Cox proportional hazard models with time-dependent covariates	Pneumonia‡ (adjusted) Dementia severity (BANS-S* at every assessment) Time between assessments of BANS-S* Time until pneumonia Time from pneumonia until survival/censored time	Mortality	**4.6** (1.2-6.2), <0.001; 1.5, 0.155
(3b) Direct relationship between intake problems and mortality	Cox proportional hazard models with time-dependent covariates	Intake problem‡ (unadjusted) Time until intake problem Time from intake problem until survival/censored time	Mortality	**10.2** (7.7-13.5), <0.001; 2.32, 0.144
(3b +) Whether the dementia severity changed the strength of this associations	Cox proportional hazard models with time-dependent covariates	Intake problem‡ (adjusted) Dementia severity (BANS-S* at every assessment) Time between assessments of BANS-S* Time until intake problem Time from intake problem until survival/censored time	Mortality	**6.2** (6.1-11.3), <0.001; 2.12, 0.155
(4a) Relation between pneumonia and intake problems	Cox proportional hazard models with time-dependent covariates	Pneumonia Time until pneumonia Time until intake problem Survival time/censored time	Intake problem	**1.7** (1.0-2.8), 0.036; 0.54, 0.252
(4b) Relation between intake problems and pneumonia	Cox proportional hazard models with time-dependent covariates	Intake problems Time until intake problem Time until pneumonia Survival time/censored time	Pneumonia	**3.1** (1.9-5.1), <0.001; 1.13, 0.253
(5a) Whether pneumonia mediated the relationship between the severity of dementia and mortality	Product method of Sobel	Pneumonia‡ Coefficients of 2a/3a		0.025

TABLE 1. (*continued*)

Association	Method	Time-dependent Covariates	Dependent Variables	HR (95% CI), *P*; Coefficient, SE
(5b) Whether intake problems mediated the relationship between the severity of dementia and mortality	Product method of Sobel	Intake problems‡ Coefficients of 2b/3b		< 0.001

Clustering of residents within long-term care facilities is taken into account in all models. The HR are bolded.
*BANS-S = Bedford Alzheimer Nursing Severity-Scale (range, 7 to 28, with higher scores indicating more severe dementia).
†Advanced dementia = a Global Deterioration Scale score of 7 and a Cognitive Performance Scale of 5 of 6.
‡38 patients developed both pneumonia and an intake problem. These patients were included in both variables that concerned pneumonia and variables that concerned intake problems.

these 2 associations, we added the longitudinal BANS-S scores to the Cox models (3a +, 3b +). Fourth, we explored the relation between the development of pneumonia and intake problems (4a), and vice versa (4b), with Cox proportional hazard models with time-dependent covariates. To assess whether pneumonia and intake problems mediated the relationship between the severity of dementia and mortality (5a, 5b), we used the product method to compute indirect effects and the Sobel test to assess significance.[31–33] The strength of relationships was expressed in terms of hazard ratios (HR) and statistical significance level was set to 0.05. To account for clustering of residents within 34 long-term care facilities, we adjusted for clustering all the analyses, and reported these results. The analyses were performed using R software version 3.0.2,[34] and IBM SPSS 20.0 (SPSS 2011).

RESULTS

Resident Characteristics

Of all residents (N = 372), 10 (3%) were lost to follow-up, due to moving to another long-term care facility, or due to the physician withdrawing from collecting data. In 34 cases (9%), residents died shortly after admission, and therefore the physicians had no chance to complete the baseline assessment. Of all newly admitted residents, 58% were admitted from their own home or from a residential home. The most important reasons for admission were neuropsychiatric symptoms, physical health problems, and distress of the caregiver. The most common type of dementia was Alzheimer disease (46%). The median BANS-S score at baseline was 13.0, with a range from 7 to 28 covering the theoretical range (7 to 28) of the BANS-S scores. Of the residents, 25% had a BANS-S score of 7 to 9, which implies that those residents were not completely dependent for any of the ADL items (bed mobility, transfer, locomotion on unit, dressing, eating, toilet, personal hygiene). The median CPS score was 3.0, 88% had a GDS score of < 7, and only 9% of the residents had advanced dementia upon admission. The median score of ADL functioning was 10 (range, 0 to 28) (Table 2).

The Relationship Between Pneumonia, Intake Problems, and Severity of Dementia

During follow-up, 103 (28%) residents developed pneumonia, 126 (34%) residents developed intake problems, and 38 (10%) developed both pneumonia and an intake problem. The most important symptoms and health conditions of the residents with pneumonia and/or intake problems are shown in Tables 3 and 4. The hazard rate of developing pneumonia in the first year was 0.27 (95% CI, 0.20-0.33), and the hazard rate of developing intake problems in the first year was 0.29 (95% CI, 0.23-0.35).

At baseline there were no significant differences in BANS-S scores and proportion of advanced dementia between the residents who did or did not develop pneumonia. The median BANS-S score before developing a pneumonia was 14.0 (range, 7 to 24; 20% of the residents had a BANS-S score of 7 to 9). More severe dementia, in terms of BANS-S scores, was significantly associated with a higher risk of developing pneumonia, the HR per point increment BANS-S score was 1.07 [95% CI, 1.01-1.14; Table 1 (2a) and Fig. 1].

Residents who developed an intake problem had more severe dementia at baseline (a higher BANS-S score, mean difference 1.5, 95% CI, 0.6-2.4), than residents who did not, but there was no significant difference in the proportions of advanced dementia. The median BANS-S score before developing an intake problem was 15.5 (range, 7 to 23; 13% of the residents had a BANS-S score of 7 to 9). More severe dementia was associated with a higher risk of developing intake problems, with a HR of 1.16 per point increment BANS-S score [95% CI, 1.10-1.23; Table 1 (2b) and Fig. 1].

Mortality and the Mediation of Pneumonia and Intake Problems

During follow-up, 227 (61%) residents died with a median survival time of 8.4 months (25th percentile = 3.9, 75th percentile = 17.3). For the first year after admission, the hazard rate of mortality was 0.45 (95% CI, 0.37-0.53). Residents who died had more severe dementia at baseline than the residents who survived during follow-up (a higher BANS-S score, mean difference 2.9, 95% CI, 2.1-3.8, and a corresponding larger proportion had advanced dementia: 12% vs. 4%, $\chi^2 = 5.3$, $P = 0.022$). Overall, the median increment in BANS-S score in 1 year was 1.3 (25th percentile = 0.0, 75th percentile = 3.0). Over the follow-up period, more severe dementia was significantly associated with a higher mortality risk, the HR per point increment BANS-S score was 1.19 [95% CI, 1.14-1.23; Table 1 (1) and Fig. 1].

Of the 103 residents with pneumonia, 75 (73%) died during follow-up with a median survival time of 5 weeks since the development of pneumonia, and of the 126 residents with an intake problem, 101 (80%) residents died, with a median survival time of 4 weeks since the development of intake problems. Pneumonia and intake problems were significantly associated with mortality. When the association between pneumonia and mortality was adjusted for the BANS-S score, the HR remained similar with a

TABLE 2. Resident Characteristics

Characteristics at Baseline = Assessment 8 wk After Admission	Total Population (N = 372) n/N*	%
Female	260/372	70
Age [median (range)]	372/372	84.5 (79.9-88.2)
Residence before admission		
Private home	117/364	32
Residential home	96/364	26
Other nursing home	56/364	15
General/psychiatric hospital	70/364	19
Other	25/364	7
2 most important reasons for admission		
Neuropsychiatric symptoms	227/355	64
Physical health problems	203/355	57
Distress of caregiver	144/355	41
Other reasons	5/355	1
Type of dementia		
Alzheimer disease	167/363	46
Vascular	82/363	23
Alzheimer and vascular	67/363	18
Lewy body/Parkinson disease	19/363	5
Other types or combinations	28/363	8
Advanced dementia†	28/329	9
CPS [median (25th percentile, 75th percentile)]	323/372	3.0 (3.0, 5.0)
Score 0, 1, or 2	70/323	22
Score 3 or 4	143/323	44
Score 5 or 6	110/323	34
GDS score of 7	39/328	12
BANS-S [median (25th percentile, 75th percentile)]‡	362/372	13.0 (9.0, 17.0)
ADL functioning [median (25th percentile, 75th percentile)]§	359/372	10 (5, 19)
Illness Severity Score [median (25th percentile, 75th percentile)]‖	326/372	2 (1, 5)
Nutritional status cachectic¶	46/326	14
Hydration status dehydrated#	23/327	7
Weight loss**	33/310	11
Characteristics Shortly Before Dying = A Maximum of 6 mo Before Death	**Total Residents Who Died During Follow-up (N = 227)**	
	n/N	**%**
Advanced dementia in the last month of life†	80/210	38
CPS [median (25th percentile, 75th percentile)]	209/227	5 (3, 5)
Score 0, 1, or 2	16/209	8
Score 3 or 4	63/209	30
Score 5 or 6	130/209	62
GDS score of 7	78/210	41
BANS-S [median (25th percentile, 75th percentile)]‡	200/227	16.0 (13.0, 19.0)
Median time until death (25th percentile, 75th percentile) (wk)	199/227	12 (3, 19)

*In some cases, the total number refers not to 372 residents, because of 34 residents died before or shortly after the baseline assessment and therefore the physicians had no chance to complete the baseline assessment prospectively, or because of missing values. We used a shortened baseline assessment to complete only the data of resident characteristics that we deemed not particularly vulnerable to recall bias.

†Advanced dementia = a Global Deterioration Scale score of 7 and a Cognitive Performance Scale of 5 of 6.

‡BANS-S = Bedford Alzheimer Nursing Severity-Scale (theoretical range, 7 to 28, with higher scores indicating more severe dementia); the range of BANS-S scores at baseline was 7 to 28.

§ADL-functioning = Activities of Daily Living Scale-Long Form (range, 0 to 28, with higher scores indicating more dependency).

‖Illness Severity Score = scores range from 1 to 9, with higher scores indicating more severe illness.

¶Nutritional status, cachectic = cachectic (very cachectic/cachectic) or not cachectic (normal/adipeus/very adipeus).

#Hydration status, dehydrated = dehydrated (mildly dehydrated/dehydrated/severely dehydrated) or not.

**Weight loss = weight loss of $\geq 5\%$ in last month, or $\geq 10\%$ in the last 6 months.

CPS indicates Cognitive Performance Scale; GDS, Global Deterioration Scale.

change from 4.1 (95% CI, 3.1-5.4) to 4.6 [95% CI, 1.2-6.2; Table 1 (3a, 3a +) and Fig. 1]; similarly, when the association between intake problems and mortality was adjusted for the BANS-S score, the HR changed from 10.2 (95% CI, 7.7-13.5) to 6.2 [95% CI, 6.1-11.3; Table 1 (3b, 3b +) and Fig. 1]. Moreover, using the product method of Sobel, we found that the relationship between the severity of dementia and death was significantly mediated by both the development of pneumonia ($P = 0.025$) and intake problems [$P < 0.001$; Table 1 (5a, 5b) and Fig. 1].

TABLE 3. The Median Length of Time Until the First Pneumonia, Symptoms, and Health Condition (n = 103)

Items*	n/N†	%
Median length of time from admission to pneumonia (25th percentile, 75th percentile) (mo)	103/103	6.5 (2.2, 15.7)
Advanced dementia at baseline‡	5/93	5
Advanced dementia before pneumonia‡,§	12/74	16
BANS-S score at baseline [median (25th percentile, 75th percentile)]‖	101/103	13.0 (9.0, 16.7)
BANS-S score before pneumonia [median (25th percentile, 75th percentile)]§,‖	75/103	14.0 (10.0, 18.0)
X-ray performed (and positive)¶	4/90	4
Sputum examination performed	1/90	1
Blood examination performed	17/91	19
(Suspected) cause aspiration	25/88	28
Systolic blood pressure assessed	51/89	57
Mean (SD)	49/51	123 (23)
Pulse rate per minute, assessed	70/98	71
Mean, per minute (SD)	77/79	90 (17)
Temperature, assessed#	86/99	87
Mean (SD) (°C)	85/86	38.2 (0.8)
Respiratory rate per minute, assessed	38/94	40
Mean rate, per minute (SD)	37/38	31 (10)
Dyspnea	72/98	73
Decreased alertness	40/97	41
Decubitus	4/97	4
Min 1.5 L/d drunk in last week	43/92	47
Eating dependency		
Independent	20/94	21
Requires assistance	45/94	48
Fully dependent	29/94	31
Risk score, mean (SD)**	60/89	13.8 (4.6)
Estimated risk of death within 14 d**	60/89	16

*Because of the observational nature, the physicians were not requested to perform additional assessments for purpose of the study.

†Total number does not refer to total number of 103, because of missings, and because 22 residents developed the first pneumonia before the baseline assessment. The number refers to the cases who developed the first pneumonia. This includes 38 residents who also developed an intake problem.

‡Advanced dementia = a Global Deterioration Scale score of 7 and a Cognitive Performance Scale of 5 of 6.

§Assessment was maximal 6 months before developing pneumonia.

‖BANS-S = Bedford Alzheimer Nursing Severity-Scale (theoretical range, 7 to 28, with higher scores indicating more severe dementia); the range of BANS-S scores at baseline was 7 to 24; 20% of the residents had a BANS-S score of 7 to 9, which implies that those residents were not completely dependent for any of the ADL items.

¶X-ray was obtained for 4 residents, which were all positive for pneumonia.

#Temperature was assessed rectally in 73%, auricularly 22%, and axillary 5%.

**Risk score to estimate risk of death within 14 days in patients with pneumonia, and dementia when treated with antibiotics (89 residents received antibiotics of whom 60 had completed data for estimating the risk score).

TABLE 4. The Median Length of Time Until the First Intake Problem, Health Condition, and Primary Reason for the Intake Problem (N = 126)

Items	n/N*	%
Median length of time from admission to intake problem (25th percentile, 75th percentile) (mo)	125/126	7.6 (2.3, 17.0)
Advanced dementia at baseline†	11/109	10
Advanced dementia before intake problem†,‡	17/94	18
BANS-S score at baseline [median (range)]§	126/126	14.0 (10.0,18.0)
BANS-S score before intake problem [median (25th percentile, 75th percentile)]‡,§	96/126	15.5 (12.0, 19.0)
New acute medical illness	32/119	27¶
Became too weak or large decline	25/119	21
Refusal to eat or drink but unknown cause	20/119	17
Swallowing problem	13/119	11
No appetite	12/119	10
Unexplained decrease oral intake or weight loss	11/119	9
Unable to eat independently	10/119	8
Chewing problem	9/119	8
Refusals to eat or drink because of suspected depression	7/119	6
Eating apraxia	6/119	5
Other reasons (eg, teeth problems, nausea)	18/119	15

*Total number does not refer to total number of 126, because of missings, and because 23 residents developed the first intake problem before the baseline assessment. The number refers to the cases when residents developed a first intake problem. This includes the 38 residents who also developed pneumonia.

†Advanced dementia = a Global Deterioration Scale score of 7 and a Cognitive Performance Scale of 5 of 6.

‡Assessment was maximum of 6 months before developing an intake problem.

§BANS-S = Bedford Alzheimer Nursing Severity-Scale (theoretical range, 7 to 28, with higher scores indicating more severe dementia); the range of BANS-S scores at baseline was 7 to 23; 13% of the residents had a BANS-S score of 7 to 9, which implies that those residents were not completely dependent for any of the ADL items). The BANS-S includes an eating item (degree of dependency); however, "unable to eat independently" was the underlying cause of intake problems in only 8% of cases.

¶Total percentages do not refer to total number of 119, because more reasons per resident were possible.

DISCUSSION

To the best of our knowledge, this is the first prospective study exploring how pneumonia and intake problems affect survival in patients with dementia admitted to a long-term care facility. It is also the first study that explores whether and how dementia severity is related to pneumonia, intake problems, and mortality in nursing home residents. We show that after admission, residents frequently developed pneumonia and intake problems, which in turn were important risk factors for mortality, regardless of the stage of dementia. Intake problems and pneumonia were more strongly associated with mortality than severity of dementia. Further, compared with pneumonia, intake problems were a more important risk factor for mortality, and were also more strongly related to more severe dementia in nursing home residents.

Mitchell et al[5] reported eating or drinking problems in 85.8%, and pneumonia in 41.4% of residents with advanced dementia (CPS score of 5 or 6 and GDS score of 7) during a study period of 18 months. Pneumonia and intake problems are regarded as hallmarks of the advanced stage of dementia, and it is generally accepted that in case of advanced dementia palliation is a reasonable primary goal of care.[1,5,35] Our study shows that residents with less advanced dementia (BANS-S scores range, 7 to 24; CPS < 5 and GDS < 7) also frequently developed pneumonia and intake problems, in line with recently reported findings from an after-death study.[36]

Dementia severity is a risk factor for mortality in nursing home residents with dementia, but pneumonia and

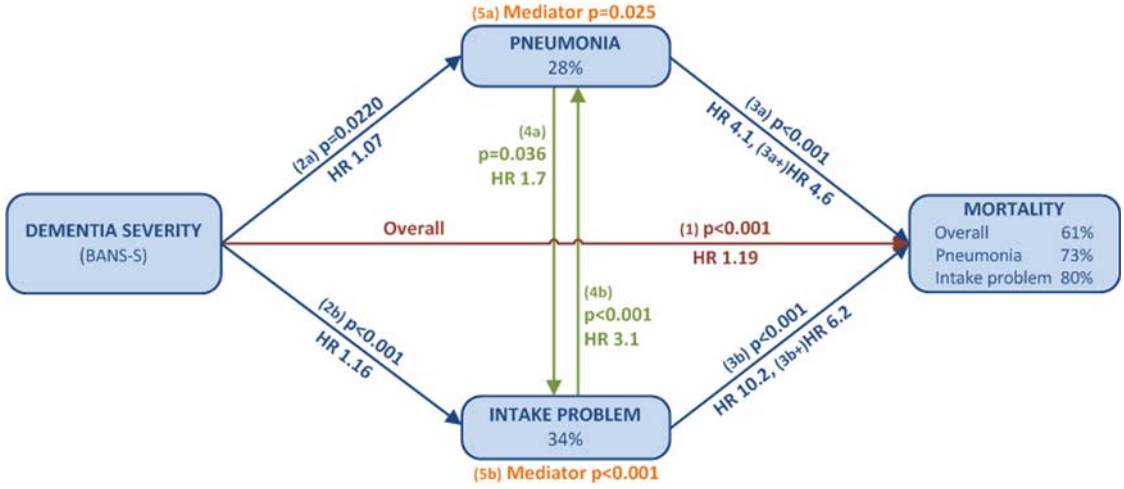

FIGURE 1. Model of the relationships between dementia severity, pneumonia, intake problems, and mortality. Note that Table 1 presents detail about the modeling of the relationships. HR indicates hazard ratio. full color online

intake problems were found to be even more important risk factors and were both partly dependent on dementia severity. Our study found that almost 3 per 10 residents developed at least 1 pneumonia in the first year, and of the residents who died (after developing a pneumonia) during follow-up the median survival time was just 5 weeks. Even so, 3 per 10 residents developed an intake problem in the first year and of the residents who died, the median survival time was just 4 weeks. Other studies also concluded that pneumonia and intake problems often occur in patients with dementia, and are associated with poorer survival; however, these studies are limited to advanced dementia, or limited to patients who developed a pneumonia.[35,37,38] We found that compared with pneumonia, intake problems are more strongly associated with both the progression of dementia and mortality.

Strengths and Limitations

Our study is unique in that we performed longitudinal survival analyses and studied jointly the severity of the dementia, pneumonia, and intake problems. Pneumonia diagnoses were based on clinical judgment and in most cases not confirmed by x-ray. However, as this is consistent with usual diagnostic procedures in Dutch primary care and long-term care[26] and elsewhere,[39] it increases the relevance for the clinical practice. Some limitations should be acknowledged. First, this study is limited to residents who were newly admitted to a long-term care facility. Therefore, our findings may not be generalizable to patients who live in the community; however, our study population consists of nursing home residents with variable stages of dementia (the range of BANS-S scores covers the theoretical range of the BANS-S scores) and who were just newly admitted to a long-term care facility. In addition, the majority of people with dementia in the United States and Western Europe are admitted to or die in long-term care facilities.[40] Second, our definition of intake problems includes different underlying causes of intake problems (eg, new acute medical illness, became too weak or strong decline, swallowing problem). The associations we found for intake problems may differ in strength for different underlying causes of intake problems, but subgroup analyses were not feasible because of small numbers in each category. In addition, the BANS-S includes an eating item (degree of dependency), which may have influenced the association with intake problems. However, "unable to eat independently" was the underlying cause of intake problems in only 8% of cases. Third, joint models could not be used to model all the longitudinal covariates because the JM R package cannot handle dichotomous time-dependent covariates.[30] Fourth, because not all the relationships were estimated by joint models, it was not possible to test the strength of the mediation of pneumonia and intake problems by comparing C-coefficients of models with and without the mediator. Therefore, we used the product method to compute indirect effects, which is also an accepted method of mediation. Finally, proposed mechanisms for increased mortality due to pneumonia in dementia include swallowing problems, poor dentition, decreased mobility, and impaired immune function, which presumably are also related to intake problems.[38,41] However, the statistical power was limited for the analyses of interrelation between pneumonia and intake problems, because only 38 residents had both pneumonia and intake problems.

Recommendations

Dementia is a disease without cure and following nursing home admission, residents of dementia special care units have a high risk of developing pneumonia and intake problems with poor survival. Moreover, developing pneumonia and intake problems involved elevated levels of suffering and might be the most common end-of-life complications.[4,8,42,43] Therefore, developing pneumonia and intake problems are import signals to consider palliative care actions.

Our findings may also have implications for the timing and initiation of advance care planning. Preferably, advance care planning should start directly after nursing home admission, or perhaps even earlier, provided that people are open and willing to look ahead and plan for the future.[9] In any case, our study suggests that we should not wait until the stage of advanced dementia. Providing accurate information about the course of dementia and expected health problems may facilitate adequate palliative

care for nursing home residents with dementia, and may help patients and families prepare for the future.

Future studies may explore whether patients and their families are receptive to start advance care planning in an early phase of the disease, and how advance care planning could be facilitated in an early phase. Further, there is a strong policy tendency to postpone nursing home admission as long as possible. As a consequence, there will be more and more patients living at home and treated in primary care with more severe stages of dementia. Therefore, future studies may investigate whether a palliative care approach is also relevant in patients with dementia in primary care.

CONCLUSIONS

Pneumonia and intake problems are not limited to, or typical of, advanced dementia. Moreover, these health problems are important risk factors for mortality in nursing home residents in all stages of dementia. The high risk of developing pneumonia and intake problems, and the poor survival of residents with dementia in a long-term care facility even shortly after admission, call for a palliative care approach and an active focus on advance care planning upon nursing home admission, or preferably earlier. Informing patients and families about the course of dementia and expected health problems may help to formulate realistic care goals and to translate these goals into appropriate palliative care. Addressing palliative care needs may benefit residents in all stages of dementia and should not be a privilege for patients with advanced dementia only.

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REFERENCES

1. van der Steen JT, Radbruch L, Hertogh CM, et al. White paper defining optimal palliative care in older people with dementia: a Delphi study and recommendations from the European Association for Palliative Care. *Palliat Med*. 2014;28:197–209.
2. Houttekier D, Cohen J, Bilsen J, et al. Place of death of older persons with dementia. A study in five European countries. *J Am Geriatr Soc*. 2010;58:751–756.
3. van der Steen JT, Ribbe MW, Deliens L, et al. Retrospective and prospective data collection compared in the Dutch End Of Life in Dementia (DEOLD) study. *Alzheimer Dis Assoc Disord*. 2014;28:88–94.
4. Vandervoort A, Van den Block L, van der Steen JT, et al. Nursing home residents dying with dementia in Flanders, Belgium: a nationwide postmortem study on clinical characteristics and quality of dying. *J Am Med Dir Assoc*. 2013;14:485–492.
5. Mitchell SL, Teno JM, Kiely DK, et al. The clinical course of advanced dementia. *N Engl J Med*. 2009;361:1529–1538.
6. Volicer L, Seltzer B, Rheaume Y, et al. Eating difficulties in patients with probable dementia of the Alzheimer type. *J Geriatr Psychiatry Neurol*. 1989;2:188–195.
7. Teno JM, Coppola KM. For every numerator, you need a denominator: a simple statement but key to measuring the quality of care of the "dying". *J Pain Symptom Manage*. 1999;17:109–113.
8. Hendriks SA, Smalbrugge M, Hertogh CM, et al. Dying with dementia: symptoms, treatment, and quality of life in the last week of life. *J Pain Symptom Manage*. 2014;47:710–720.
9. Hertogh CM. Advance care planning and the relevance of a palliative care approach in dementia. *Age Ageing*. 2006;35:553–555.
10. Koopmans RT, van der Sterren KJ, van der Steen JT. The'natural' endpoint of dementia: death from cachexia or dehydration following palliative care? *Int J Geriatr Psychiatry*. 2007;22:350–355.
11. Vandervoort A, Houttekier D, Van den Block L, et al. Advance care planning and physician orders in nursing home residents with dementia: a nationwide retrospective study among professional caregivers and relatives. *J Pain Symptom Manage*. 2014;47:245–256.
12. van der Steen JT. Dying with dementia: what we know after more than a decade of research. *J Alzheimers Dis*. 2010;22:37–55.
13. Todd S, Barr S, Roberts M, et al. Survival in dementia and predictors of mortality: a review. *Int J Geriatr Psychiatry*. 2013;28:1109–1124.
14. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34:939–944.
15. Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. *Neurology*. 1993;43:250–260.
16. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology*. 1996;47:1113–1124.
17. van der Steen JT, Volicer L, Gerritsen DL, et al. Defining severe dementia with the Minimum Data Set. *Int J Geriatr Psychiatry*. 2006;21:1099–1106.
18. Morris JN, Fries BE, Morris SA. Scaling ADLs within the MDS. *J Gerontol A Biol Sci Med Sci*. 1999;54:M546–M553.
19. Oye RK. A simple method for rating illness severity at admission and expected functional status at discharge: how should we use the information? *Am J Med*. 2000;109:250–251.
20. Charlson ME, Hollenberg JP, Hou J, et al. Realizing the potential of clinical judgment: a real-time strategy for predicting outcomes and cost for medical inpatients. *Am J Med*. 2000;109:189–195.
21. Health Care Financing Administration. *Long-Term Care Facility Resident Assessment Instrument (RAI) User's Manual*. Washington, DC: Health Care Financing Administration; 1995.
22. Volicer L, Hurley AC, Lathi DC, et al. Measurement of severity in advanced Alzheimer's disease. *J Gerontol*. 1994;49:M223–M226.
23. Bellelli G, Frisoni GB, Bianchetti A, et al. The Bedford Alzheimer Nursing Severity scale for the severely demented: validation study. *Alzheimer Dis Assoc Disord*. 1997;11:71–77.
24. Reisberg B, Ferris SH, de Leon MJ, et al. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982;139:1136–1139.
25. Morris JN, Fries BE, Mehr DR, et al. MDS Cognitive Performance Scale. *J Gerontol*. 1994;49:M174–M182.
26. van der Steen JT, Mehr DR, Kruse RL, et al. Predictors of mortality for lower respiratory infections in nursing home residents with dementia were validated transnationally. *J Clin Epidemiol*. 2006;59:970–979.
27. EMGO Institute. *The Risk Score for Patients With Pneumonia and Dementia Explanation and Background*. Amsterdam: VU University Medical Center; 2010. Available at: http://www.emgo.nl/files/119.2010. Accessed January 19, 2016.
28. EMGO Institute. *Risk Score in Pneumonia and Dementia*. Amsterdam: VU University Medical Center; 2008. Available at: http://www.emgo.nl/files/105. Accessed January 19, 2016.
29. Byrne EJ, Benoit M, Lopez Arrieta JM, et al. For whom and for what the definition of severe dementia is useful:

an EDCON consensus. *J Nutr Health Aging*. 2008;12: 714–719.
30. Rizopoulos D. *Joint Models for Longitudinal and Time-to-Event Data With Applications in R Joint Models for Longitudinal and Time-to-Event Data*. Boca Raton: Chapman and Hall/CRC Biostatistics Series; 2012.
31. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods*. 2008;40:879–891.
32. Sobel ME. Asymptotic intervals for indirect effects in structural equations models. *Social Methodol*. 1982;13:290-312.
33. Preacher KJ, Leonardelli GJ. Calculation for the Sobel test. An interactive calculation tool for mediation tests; 2014. Available at: http://www.quantpsy.org/sobel/sobel.htm. Accessed January 19, 2016.
34. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2013. Available at: http://www.R-project.org/ Accessed. Accessed January 19, 2016.
35. Mitchell SL, Kiely DK, Hamel MB, et al. Estimating prognosis for nursing home residents with advanced dementia. *JAMA*. 2004;291:2734–2740.
36. Vandervoort A, Houttekier D, Vander SR, et al. Quality of dying in nursing home residents dying with dementia: does advanced care planning matter? A nationwide postmortem study. *PLoS One*. 2014;9:e91130.
37. Hanson LC, Ersek M, Lin FC, et al. Outcomes of feeding problems in advanced dementia in a nursing home population. *J Am Geriatr Soc*. 2013;61:1692–1697.
38. van der Steen JT, Ooms ME, Mehr DR, et al. Severe dementia and adverse outcomes of nursing home-acquired pneumonia: evidence for mediation by functional and pathophysiological decline. *J Am Geriatr Soc*. 2002;50:439–448.
39. Helton MR, Cohen LW, Zimmerman S, et al. The importance of physician presence in nursing homes for residents with dementia and pneumonia. *J Am Med Dir Assoc*. 2011;12:68–73.
40. Reyniers T, Deliens L, Pasman HR, et al. International variation in place of death of older people who died from dementia in 14 European and non-European countries. *J Am Med Dir Assoc*. 2015;16:165–171.
41. Kelaiditi E, Demougeot L, Lilamand M, et al. Nutritional status and the incidence of pneumonia in nursing home residents: results from the INCUR study. *J Am Med Dir Assoc*. 2014;15:588–592.
42. van der Steen JT, Ooms ME, Van der WG, et al. Pneumonia: the demented patient's best friend? Discomfort after starting or withholding antibiotic treatment. *J Am Geriatr Soc*. 2002;50: 1681–1688.
43. van der Maaden T, van der Steen JT, de Vet HC, et al. Prospective observations of discomfort, pain, and dyspnea in nursing home residents with dementia and pneumonia. *J Am Med Dir Assoc*. 2016;17:128–135.