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Original Study

Determinants of Mortality and Causes of Death in Patients With Dementia and Very Severe Challenging Behavior

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A B S T R A C T

Objectives: To gain insight into the mortality over time of patients with very severe challenging behavior in dementia when they are temporarily admitted to highly specialized units for treating the behavior.
Design: Observational study.
Setting and Participants: Eleven highly specialized units throughout the Netherlands participated from December 2020 until December 2022, with a follow-up in September 2023, with 127 patients participating.
Methods: General clinical characteristics were collected, such as demographics and cognitive functioning, behavior during the first 2 weeks assessed by the Cohen-Mansfield Agitation Inventory (CMAI) and the Neuropsychiatric Inventory Questionnaire (NPI-Q), date of death, and cause of death. Two Cox regression models were estimated, namely prediction models to describe the relationship between some (regular) determinants and mortality over time and association models between behavioral factors and mortality.
Results: Of the 127 participants, one-third died during their stay. The most prevalent causes of death were dehydration (often with cachexia) and pneumonia. Mortality over time is best predicted by age (ie, being 80 years or older) and the number of non-psychotropic drugs, as a proxy for somatic disease burden. The 10% of patients scoring highest on the CMAI factor of physically aggressive behavior had a ninefold increased mortality risk during their stay.
Conclusions and Implications: A considerable number of patients with very severe challenging behavior in dementia admitted to highly specialized units died during their stay, with a ninefold increased mortality risk over time found in patients with very severe physical aggression. This underlines the need to devote attention to suitable terminal palliative care in clinical practice and research in this patient group.

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Dementia significantly shortens life expectancies.[1] In persons with dementia living in nursing homes, the most common causes of death are drinking and/or eating problems and pneumonia, with most deaths occurring in severe dementia stages before the final stage.[2-4] Commonly reported causes of death for persons with dementia are respiratory- or circulatory-related problems.[5] Determinants of mortality in persons with dementia include higher age, male sex, chronic somatic conditions, increased drug use, dementia type, more severe dementia stages, delirium, and psychiatric history.[6-12] Interestingly, challenging behavior has also been associated with higher mortality rates when assessed by the neuropsychiatric inventory (NPI).[10,13,14]

In the Netherlands, highly specialized units for the temporary treatment of patients with dementia and very severe challenging behavior have been established in the past decade. These units were developed for situations in which care and treatment in a regular dementia special care unit (DSCU) are no longer possible because of the behavior's severity or danger.[15] There is some variation in the allowance of the number of patients with severe physical aggression and alcohol dependency.[15] These units are organized within a long-term care organization, that is, an organization with nursing home facilities, a mental health care organization, and sometimes a collaboration of both. The median length of stay in these units was 5 months.[15] Because these units are relatively new, they are pioneering in their organization and treatment. Similarities among specialized units include observation with an open attitude, the key role of nursing staff, frequent multidisciplinary meetings, and attention to sensory stimuli.[15] Comparable units also exist in Australia and the United Kingdom, albeit with different organization and reimbursement most likely due to differences in health policies.[16-18]

Very severe challenging behavior is more commonly found in persons in more severe dementia stages,[19,20] and knowledge about mortality in persons with dementia and very severe challenging behavior is scarce. In recent research, a sevenfold higher 1-year mortality risk was found among patients with dementia and severe aggression incidents within the first 48 hours of a stay in a specialized psychogeriatric ward in a psychiatric hospital.[21] The context of these highly specialized units offers a unique opportunity to investigate the characteristics of persons with dementia and very severe challenging behavior. Most studies in persons with dementia and challenging behavior include persons among the general population. For severe challenging behavior, scores on a measurement scale—for instance, severity of neuropsychiatric symptoms[19] or frequency of agitation[20]—are typically used rather than a clinically relevant event such as admission to these highly specialized units.

This study aims to (1) gain more insights into causes of death in patients with dementia and very severe challenging behavior; (2) explore the previously identified determinants of mortality in dementia during a stay in a highly specialized unit; and (3) explore the association between specific subtypes of very severe challenging behavior and mortality during a stay. We hypothesized that the severity of challenging behavior adds to the predictive value of previously known determinants of mortality in dementia, that is, higher age, male sex, chronic somatic conditions, delirium, and psychiatric history.[6,7,9-12]

Methods

Study Design

Design

This observational study followed patients from admission to a highly specialized unit until discharge or death. For newly admitted participants, demographics, clinical characteristics, behavior during the first 2 weeks of stay, and details about discharge or death, including causes of death, were collected. The study took place from December 2020 to December 2022 with a follow-up 9 months after the study (September 2023). A more detailed description can be found in our paper describing patient characteristics at admission.[22]

Setting

Fifteen units treating patients with dementia and very severe challenging behavior were asked to participate, recruited within the 6 academic networks of long-term care[23] and through the network of these highly specialized units.[18] Eleven of the 15 identified units consented to participate, located throughout the Netherlands. We included *"units where patients with dementia and challenging behavior can stay temporarily for diagnosis and treatment."* In one unit both patients with dementia and severe challenging behavior and those with cognitive or geriatric psychiatric problems could be admitted. Unit sizes ranged from 7 to 28 places. Seven units were part of a long-term care organization, 2 were part of a mental health care organization, and 2 were a cooperation of a long-term care and a mental health care organization.

Participants

Newly admitted patients were eligible if they had (1) dementia or suspected dementia, and (2) very severe challenging behavior, defined according to the Dutch guideline as severe verbal or physical aggression, agitation, and/or vocally disruptive behavior *"associated with suffering or danger to the person or people in his or her environment."*[24] Exclusion criteria were (1) having acquired a brain injury without (suspected) dementia, and (2) having a life expectancy of less than 2 weeks. The treating physician considered the eligibility criteria after having received an instruction. This physician was instructed to register all patients admitted to the unit during the study to gain insights into the participation rate and could consult the research team in case of doubt. We aimed to secure 200 participants to include approximately 4 variables in the models with an expectation of 40 events, that is, we expected 20% mortality based on a study describing organizational characteristics of highly specialized units and using the rule of thumb of 1 variable per 10 events.[15,25]

Data Collection and Sources

Data were collected at admission, after 2 weeks, and at discharge or after death. A follow-up about discharge or death was undertaken 9 months after the study (see later in this section). The treating physician provided details about demographics, presence of delirium, medical history, (psychotropic) drug use, and cognitive functioning at admission. Demographics, medical history including dementia type and psychiatric diagnoses, and drug use at admission were extracted from medical files, whereas delirium and cognitive functioning at admission were based on physician assessments (see Assessments). Castor EDC (https://www.castoredc.com/) was used for data management.

Two weeks after admission, a nursing staff member who was substantially involved in the patient's care during these weeks completed a digital questionnaire with validated assessment scales for challenging behavior (see CMAI and NPI). They completed the questionnaires based on their own observations, and reports from other nursing staff members in the nursing files. A staff member provided details about the discharge date and location or death during the stay. For participants who died during their stay, the physician completed a questionnaire about the cause of death.

A follow-up was undertaken 9 months after the end of the study (September 2023), during which the physician completed questions

about the discharge date and location, or the cause of death for participants who had not yet been discharged from the unit at the end of the original study in December 2022.

Assessments

The physician assessed the presence or possible presence of delirium at admission according to the diagnostic criteria for delirium from the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), registered as present, possibly present, or not present.[26] Regular drug use was classified using the Anatomical Therapeutical Chemical classification,[27] categorized into non-psychotropic and psychotropic drugs (ie, anticonvulsants, antipsychotics, anxiolytic drugs, hypnotics and sedatives, antidepressants, and anti-dementia drugs). The physician assessed the severity of cognitive functioning at admission using the Global Deterioration Scale, ranging from no cognitive decline (stage 1) to very severe decline (stage 7).[28] Immediate causes of death were registered with the same open-ended question as used in the Dutch death certificate, and these conditions were categorized by the authors A.V. and G.v.V.

CMAI

The CMAI comprises 29 items rated on a 7-point scale (1–7) ranging from "never" to "several times an hour."[29] The CMAI has strong reliability among persons with Alzheimer's dementia[30] and older persons admitted to a geriatric psychiatry ward.[31] Content validity was demonstrated to be good.[31,32] For the CMAI, physically aggressive behavior, physically nonaggressive behavior, and verbally agitated behavior can be calculated.[33] Item scores are summed to calculate a total score for each factor.

NPI-Q

The NPI-Q includes 12 neuropsychiatric symptoms: delusions, hallucinations, agitation, depression/dysphoria, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability, aberrant motor behavior, nighttime behaviors, and appetite/eating change. The severity of each symptom for the patient is rated on a 3-point (1–3) Likert scale ranging from "mild" to "severe." The emotional distress for the nursing staff member was rated on a 6-point (0–5) Likert scale ranging from "not distressing at all" to "extremely distressing."[34] The NPI-Q has good item reliability, internal consistency in hospitalized older adults,[35] and its content validity has been found to be reasonable in persons with dementia.[34] We used 4 factor scores in our analysis: psychosis, comprising delusions and hallucinations; hyperactivity, comprising agitation, disinhibition, and irritability; affect, comprising depression/dysphoria and anxiety; and apathy, comprising apathy, nighttime behaviors, and appetite/eating change. These were based on previous research with other versions of the NPI, that is, the NPI and NPI-NH (Nursing Home).[36-38] We used the total severity scores of each item as factor scores, summed from the item severity scores.

Statistical Methods

We used descriptive statistics to describe the patient characteristics, causes of death, and behavioral factors. Statistical package SPSS (version 29) was used for the analyses. Missing data for the behavioral assessment scales (n = 15 = 11.8%) were regarded as missing at random because they were distributed among 10 units and mostly due to late registration. Missing data in psychiatric history (n = 2 = 1.6%) and (non-)psychotropic drug use (n = 13 = 10.2%) were regarded as missing at random because they were distributed over 2 and 8 units, respectively. For psychiatric history, the mode—no psychiatry history—was imputed and single imputation by linear interpolation was used for drug use. After imputation for both non-psychotropic and psychotropic drug use, paired t tests compared the variables with and without imputation, with no significant differences found. We did not impute for the behavioral factors (ie, the central determinants of the association models) because we found outliers in which imputation would lead to unreliable results. Therefore, association models were based on the 112 participants with no missing data on behavioral assessments.

Prediction of Mortality

When building a prediction model for mortality during stay, we selected a set of covariates that together might best predict mortality over time. We selected age, sex, (possible) presence of delirium, psychiatric history, psychotropic drug use, and non-psychotropic drug use as independent variables and used non-psychotropic drug use as a proxy for somatic disease burden. Psychiatric history was registered as a dichotomous variable (ie, present or not present) based on the medical history. Drug use was registered as the number of regularly used non-psychotropic and psychotropic drugs at admission. The outcome was mortality over time during stay. Variables used were events (death or censored) and time to event in days. Patients who were alive at the end of their stay or follow-up were considered censored. Considering the relatively large number of determinants compared with the number of events[25] (ie, deaths), we first checked all univariable associations with mortality. In the case of a nonlinear relationship, determinants were either transformed or categorized, representing clinically meaningful categories. This applied to age (dichotomized in younger than and older than 80 years) and psychotropic drug use (dichotomized in 2 drugs and more than and fewer than 2 drugs). The proportional hazard assumption was checked by the Kaplan-Meier curves and log-minus-log plots because interpretating Kaplan-Meier curves is partly subjective and might be misleading when sample sizes are small or censoring is high, whereas the more formal log-minus-log plots might lead to noise due to sparse events and perform poorly at extreme time points (early and late).[39] Subsequently, we used a backward elimination procedure to select a set of covariates that best predict death. We performed 2 sensitivity analyses, with one model restricted to participants with Alzheimer's dementia and one without imputed data. Finally, we internally validated our model with a bootstrap procedure.

Explorative Association Between Behavior and Mortality

Subsequently, we examined the association between behavioral characteristics (CMAI, NPI-Q) and mortality adjusted for the determinants of mortality during stay as used in the prediction model in our sample. We planned to categorize characteristics in case of nonlinear associations based on the assumption of clinical relevance for extreme scores. Based on explorative models for the nonlinear CMAI factors, we dichotomized between the highest quartile and the other 3 quartiles. Sensitivity analyses were performed by dichotomizing between the top 10% and the lower 90% based on our interest in the most severe behavior. For the NPI factors, we chose clinically interpretable cutoffs based on the distribution of the answers and the distribution of the hazard ratios with the scores. We planned a sensitivity analysis restricted to participants without delirium, considering its impact on behavior. Finally, we tested for multicollinearity in these models using variance inflation factors.

This study is reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[40] (for details, see Supplementary Table 1).

Results

Of the 11 participating units, 1 unit started 1 year later and 1 withdrew consent after 2 inclusions because of organizational problems. The median participation rate was 30% (ranging from 4% to 78%; for details, see Supplementary Table 2).

Patient Characteristics and Length of Stay

A total of 127 patients participated in this study. Two-thirds of the participants were male, about 4 in 10 had Alzheimer's dementia, and about 9 in 10 had moderately severe or severe cognitive decline. More than half of the participants were discharged, and about one-third died during their stay. One participant was lost to follow-up because the legal representative withdrew their consent. The median length of stay was 122 days for discharged patients and 84 days for deceased patients. The most common causes of death were dehydration and cachexia (42.1%) and pneumonia (15.8%; see Table 1).

Prediction of Mortality Over Time With Regular Determinants

Age, the (possible) presence of delirium, and the number of non-psychotropic drugs were statistically significantly associated with mortality over time in days during stay in univariable analyses (see Figure 1). The Kaplan-Meier curves did not cross in the latter categorical variables and the log-minus-log plots ran parallel, indicating no violation of the proportional hazards assumption (see Supplementary Figure 1). In the multivariable model, age (*P* value .014) and non-psychotropic drug use (*P* value .058) best predicted mortality over time (see Figure 1). In sensitivity analysis for Alzheimer's dementia only (n = 53), no significant variable was left although the build-up was similar (ie, the penultimate step showed a similar model with similar effect sizes). For the multivariable model, sensitivity analysis without imputation (n = 113) provided similar results. In a bootstrap procedure, a similar model was found with a comparable level of significance (*P* value .013 for age and .038 for non-psychotropic drugs).

Association of Behavior With Mortality Over Time

For the participants with the 10% highest scores in the physically aggressive factor of the CMAI, we found approximately a fourfold increased hazard ratio of mortality (4.24; CI, 1.91–9.40). When adjusted for age, delirium, number of somatic drugs, gender, psychiatric history, and psychotropic drugs, this increased to a ninefold higher risk (9.18; CI, 3.58–23.52). For the NPI factor of apathy, we found an unadjusted threefold higher hazard ratio of mortality (3.07; CI, 1.08–8.67), which became nonsignificant when adjusted (2.52; CI, 0.85–7.44). For the other factors, no significant relationship was found (see Table 2). We found no signs of multicollinearity in any of the models (all variance inflation factors <1.18).

In sensitivity analysis restricted to participants without delirium (n = 97), there were no factors for which the effect size changed relevantly and reliably in both adjusted and unadjusted models. For the factor apathy, the hazard ratio increased relevantly to 4.53 (CI, 1.07–19.28), but completely adjusted this was 3.78 (CI, 0.88–16.35). For the CMAI factor of physically aggressive—when divided into the highest 10% vs others—the hazard ratios increased to 5.30 (CI, 2.28–12.32) but was not relevantly different when adjusted, with 8.11 (CI, 3.07–21.48).

Discussion

This observational study is the first to investigate causes of death and determinants of mortality during stay in patients with dementia and very severe challenging behavior admitted for treatment to highly specialized units in the Netherlands. We found similar causes of death as in regular DSCUs,[3] with a higher age and larger number of non-psychotropic drugs best predicting mortality over time. Participants with very severe physically aggressive behavior—that is, those with the highest 10% scores on the factor of physically aggressive behavior of the CMAI—had a ninefold higher risk of mortality during their stay in a highly specialized unit. We discuss these findings as follows in further detail.

Challenging Behavior and Mortality

One in 3 patients with very severe challenging behavior in highly specialized units died during their stay, with a median stay of 84 days. We found that some traditional risk factors for mortality (ie, age, somatic disease burden, and delirium) also apply to this specific population. For the 10% of participants with very severe physically aggressive behavior, this was significantly related with a ninefold increased risk of mortality during the stay in a highly specialized unit. This is somewhat similar to the results of the study among patients with dementia and severe aggression incidents within the first 48 hours of a stay in a specialized psychogeriatric ward in a psychiatric hospital mentioned in the introduction.[21] Finally, we found a trend toward a higher mortality risk over time for the behavioral NPI-Q factor apathy, that is, patients with apathy, nighttime behaviors, and/or appetite/eating change had a higher mortality risk than patients without such factors. This risk over time was higher in participants without delirium. Apathy might be a sign of different problems, such as a symptom of depression, a symptom of declining cognition or a (not recognized) hypoactive delirium.[41,42] Especially declining cognition and delirium have a known link with higher mortality.[7,11] These findings emphasize that very severe challenging behaviors might be a sign of impending death. Although not investigated here because of the relatively small sample size, future studies should explore the role of antipsychotic use and psychotropic drug use in general, which are known to be related to several adverse events and outcomes such as sleepiness, stroke, and death.[43-45] These highly specialized settings are established for a temporary stay and treatment and aim to discharge patients to a DSCU,[15] whereas for some patients these units appear to be their place of residence during their last days. This raises the question of whether these patients can be better recognized and how appropriate terminal palliative care can be provided for them.

Clinical Implications

It is necessary to acknowledge that this is one of the first investigations into this specific group, which might also differ globally due to contextual differences, especially in countries lacking the resources of highly specialized units. Nevertheless, some lessons can be learned. First, this study has found that the mortality over time of patients with very severe challenging behavior in dementia is high. Especially patients with very severe physical aggression (ie, the 1 in 10 patients with the most severe physical aggression) were about 4 times more likely to die during their stay. Moreover, patients scoring any symptom on the NPI factor of apathy (ie, those with apathy, nighttime behaviors, and/or appetite/eating change) had a threefold increased risk over time of dying during the stay. Second, about half of the patients could be discharged from a highly specialized unit, half of them within 122 days. Finally, 1 in 10 participants stayed in these units for longer than 16 months. This might imply that highly specialized units are needed for a longer time for a small group.

Table 1
Patient Characteristics, Behavior, and Follow-up (n = 127)*

Determinants in prediction model	
Age, y	78.5 (SD 8.8)
Sex, male, n (%)	86 (67.7)
Delirium at admission, yes or possibly, n (%)	17 (13.4)
Psychiatric history,† n (%)	41 (32.3)
No. of non-psychotropic drugs‡	Median 4.6 (IQR 2.0–6.3)
No. of psychotropic drugs‡	Median 2.0 (IQR 1.0–3.0)
Dementia type n (%)	
Suspected dementia	5 (3.9)
Alzheimer's dementia	54 (41.7)
Vascular dementia	26 (20.5)
Mixed type (Alzheimer's and vascular)	15 (11.8)
Lewy body dementia	2 (1.6)
Parkinson's dementia	2 (1.6)
Frontotemporal dementia	10 (7.9)
Alcohol dementia	2 (1.6)
Not specified	12 (9.4)
Severity of cognitive decline (GDS) n (%)§	
Stage 2–4 (very mild through moderate)	10 (7.9)
Stage 5 (moderately severe)	50 (39.4)
Stage 6 (severe)	61 (48)
Stage 7 (very severe)	5 (3.9)
Factor scores behavior n (%)‖	
Factors CMAI	
Physically aggressive, highest quartile = 20.8 and over (range 9–63)**	28 (25.0)
Physically aggressive, highest 10% = 29.0 and over (range 9–63)	*10 (8.9)*
Physically nonaggressive, highest quartile = 26.0 and over (range 6–42)	30 (26.8)
Physically nonaggressive, highest 10% = 31.0 and over (range 6–42)	*9 (8.0)*
Verbally agitated (range 5–35)	Median 13.6 (IQR 9.0; 21.0)
NPI-Q factors n (%)	
Psychosis, severity score 1–2, severity score 3–6 (range 0–6)	Severity score 1–2: 34 (30.4) Severity score 3–6: 36 (32.1)
Hyperactivity, severity score 1–4, severity score 5–9 (range 0–9)	Severity score 1–4: 36 (32.1) Severity score 5–9: 56 (50.0)
Affect, 1 or more symptoms/severity (range 0–6)	67 (59.8)
Apathy, 1 or more symptoms/severity (range 0–9)	85 (75.9)
Discharge and mortality n (%)	
Discharge	71 (55.9)
No discharge yet at follow-up	15 (12.6)
Mortality	40 (31.5)
Length of stay†† Median (IQR)	
Discharged patients (n = 69)‡‡	122 days (59; 224)
Not yet discharged (n = 15)	493 days (412; 616)
Deceased patients (n = 40)	84 days (57; 195)
Immediate causes of death (n = 38)† n (%)	
Dehydration often (n = 16) with cachexia	18 (47.4)
Pneumonia	6 (15.8)
Unknown cause of mortality	4 (10.5)
COVID-19	2 (5.3)
Gastrointestinal hemorrhage	2 (5.3)
Other§§	6 (15.8)

IQR, interquartile range.
Italics show a second dichotomization of the factors "physically aggressive" and "physically nonaggressive" of the CMAI.
*Overall 6.0% missing of all variables.
†Two missing (1.6%).
‡Thirteen missing (10.2%).
§One stage 5 or 6.
‖Fifteen missing (11.8%).
**Contains 5 outliers.
††One unknown due to withdrawn consent.
‡‡Two missing discharge dates (1.6%).
§§Anemia, cardiac arrest, cardiac asthma, ileus, sepsis, status epilepticus.

Implications for Research

In this study, we have investigated the relationship between regular determinants of mortality over time and behavioral factors during the first 2 weeks of stay in highly specialized units. These initial results show the importance of addressing this knowledge gap concerning patients with dementia and the most extreme behavior. Future research might profit from international research to replicate this study with more statistical power, aiming to identify clinical subgroups within patients with very severe challenging behavior in dementia. Latent cluster analysis could be valuable for this purpose.[46] As mentioned earlier, the high mortality over time raises questions about whether admission is appropriate for some patients, whether they can be recognized, and what is needed to provide terminal palliative care for these patients. Despite not being measured in this study, it is very likely that the well-being of patients with severe challenging behavior is compromised, likewise for the persons in their direct environment (ie, other patients, nursing staff, and family caregivers).[47,48] Further insights into whether and how their well-being can be improved during a stay in a highly specialized unit are necessary.

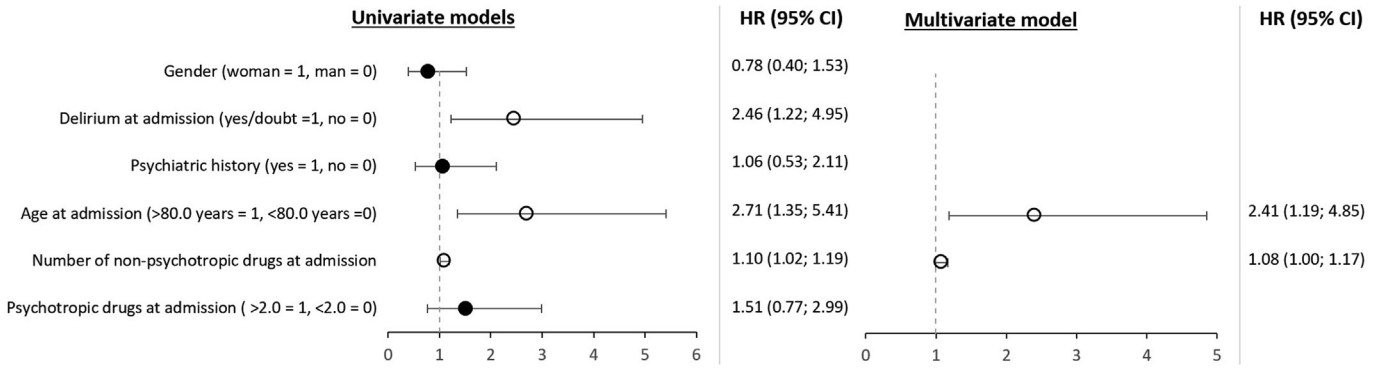

Fig. 1. Univariable and multivariable prediction models. HR, hazard ratio. • = nonsignificant, ○ = significant.

Strengths

One strength of this study is that we were able to include 11 of the 15 identified units in the Netherlands, thereby studying a relatively rare but impacting problem.

Limitations

Our explorative study has some limitations. First, although we were able to provide the overall participation rate of all admissions, we were unable to quantify whether the nonparticipants did not meet the inclusion criteria, did not consent, or were not asked to participate. Considering the reasons for the lack of these data—namely workload, vacation, and sick leave of treating physicians—selection bias is considered low. Second, we had missing data on behavioral assessment scales for 13 patients, and it is unknown whether this was related to the severity of challenging behavior. Third, determinants were only derived at admission or, for the behavioral assessment scales, after 2 weeks, implying that this study does not include how clinical diagnoses, treatment, and behavioral changes over time affect mortality over time. Insight is lacking into the role of clinical diagnoses and symptoms such as pain that might have indirectly contributed to the challenging behavior and/or death. Fourth, although using non-psychotropic drug use as a proxy for somatic disease burden is justified by evidence at the population level,[49] we do not know how reliable this is in our relatively small and specific sample. Fifth, some limitations apply to our statistical analyses. For instance, we did not perform a multilevel analysis despite that data were derived from different units within different organizations. Given our previous findings that these units are heterogeneous in their interventions used,[15] the assumption of independent observations could have been violated. We chose determinants that are known to be related to mortality over time in the prediction model and therefore might be less strongly influenced by this clustering, although this does not apply to the association models. Naturally, our explorative models should be externally validated in the future. Sixth, we did not reach our aim of 200 participants, meaning that our models are less robust than intended. Because the number of events (ie, deaths) was also higher than expected, we were still able to include 4 variables. Finally, we collected our data during the COVID-19 pandemic, which might have influenced our results. Although the number of participants who died directly from COVID-19 was limited (n = 2), we do not know to what extent the results were affected by the impacts of the pandemic.

Conclusions and Implications

This explorative observational study has found a high mortality over time in patients with dementia and very severe challenging behavior during their treatment in highly specialized units. Primary causes of death were mainly dehydration with cachexia and pneumonia. Very severe physical aggression was associated with a ninefold increase in mortality over time during a stay. This study underlines the necessity of adequate terminal palliative care in these highly specialized units.

Table 2
Association of Behavioral Factors With Mortality Over Time (n = 112)*

	Unadjusted	*P* Value	Adjusted†	*P* Value
	HR (95% CI)		HR (95% CI)	
CMAI factors				
Physically aggressive (highest quartile = 1, lowest 3 quartiles = 0)	1.54 (0.79–3.00)	.205	1.42 (0.69–2.93)	.347
Physically aggressive (highest 10% percent = 1, other 90% = 0)	**4.24 (1.91–9.40)**	**<.001**	**9.18 (3.58–23.52)**	**<.001**
Physically nonaggressive (highest quartile = 1, lowest 3 quartiles = 0)	0.74 (0.34–1.57)	.425	0.90 (0.41–1.99)	.794
Physically nonaggressive (highest 10% = 1, other 90% = 0)	1.35 (0.41–4.44)	.617	2.25 (0.63–7.99)	.211
Verbally agitated (range 5–35)	1.01 (0.97–1.05)	.556	1.01 (0.97–1.06)	.585
NPI-Q factors				
Psychosis (no symptoms = 0, severity score 1–2 = 1, severity score = 3–6 = 2)	1.03 (0.44–2.38)	.951	1.05 (0.44–2.49)	.919
	1.48 (0.69–3.18)	.309	1.9 (0.56–2.95)	.545
Hyperactivity (no symptoms = 0, severity score 1–4 = 1, severity score 5–9 = 2)	0.74 (0.25–2.20)	.582	0.88 (0.28–2.73)	.824
	1.33 (0.54–3.26)	.540	1.67 (0.67–4.16)	.276
Affect (no symptoms = 0, severity score 1–6 = 1)	0.88 (046–1.70)	.717	0.88 (0.43–1.79)	.725
Apathy (no symptoms = 0, severity score 1–9 = 1)	**3.07 (1.08–8.67)**	**.035**	2.52 (0.85–7.44)	.094

HR = hazard ratio.
Bold values indicate statistically significant ($P < .05$).
*Without the 15 missing items (11.8%) in behavioral assessment scales.
†Adjusted for age, delirium, number of somatic drugs, gender, psychiatric history, and psychotropic drug use.

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki, as well as the rules applicable in the Netherlands. The local Medical Ethics Review Committee of CMO region Arnhem-Nijmegen located at Radboud University Medical Center rated the study and stated that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study and their official approval is not required (reference number 2020-6979). Informed consent was obtained by the treating physician, who considered the patients' capacity to consent to participation in the study. Written informed consent was obtained from participants with full capacity to consent or from the legal representative of those participants with reduced capacity to consent.

Disclosure

The authors declare no conflicts of interest.

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Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2025.105713.

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