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NUTRITIONAL STATUS OF COMMUNITY-DWELLING ELDERLY WITH NEWLY DIAGNOSED ALZHEIMER'S DISEASE: PREVALENCE OF MALNUTRITION AND THE RELATION OF VARIOUS FACTORS TO NUTRITIONAL STATUS

E. DROOGSMA[1], D.Z.B. VAN ASSELT[1], C.J.M. SCHOLZEL-DORENBOS[2], J.H.M. VAN STEIJN[1], P.E. VAN WALDERVEEN[1], C.S. VAN DER HOOFT[1]

1. Geriatric Medicine, Medical Centre Leeuwarden, PO Box 888 Leeuwarden 8901 BR, The Netherlands; 2. Geriatrics, Slingeland Hospital, Doetinchem, The Netherlands. Corresponding author: : D.Z.B. Van Asselt. Tel: +(31) 582863510; Fax: +(31) 582866837. Email: dieneke.van.asselt@znb.nl

Abstract: *Objectives:* To determine the prevalence of malnutrition and its relation to various factors in community-dwelling elderly with newly diagnosed Alzheimer's disease (AD). *Design:* Retrospective cross-sectional study. *Setting:* Memory clinic in a rural part of the Netherlands. *Participants:* 312 Community-dwelling AD patients, aged 65 years or older, were included. *Measurements:* At the time the diagnosis AD was made, socio-demographic characteristics and data on nutritional status (Mini Nutritional Assessment (MNA)), cognitive function (Mini Mental State Examination (MMSE), Cambridge Cognitive Examination (Camcog)), functional status (Interview for Deterioration in Daily Living Activities in Dementia (IDDD), Barthel Index (BI)) and behaviour (Revised Memory and Behaviour Problems Checklist (RMBPC)) were assessed. Characteristics of well-nourished patients (MNA score >23.5) were compared to characteristics of patients at risk of malnutrition (MNA score 17-23.5). Linear regression analysis was performed to assess the effect of various factors on nutritional status. *Results:* The prevalence of malnutrition was 0% and 14.1% was at risk of malnutrition. AD patients at risk of malnutrition were more impaired in basic and complex daily functioning than well-nourished AD patients (median IDDD score 41.5 [25th -75th percentile 38.8-48.0] versus median IDDD score 40.0 [25th - 75th percentile 37.0-43.0], p = 0.028). The degree of impairment in basic and complex daily functioning (IDDD) was independently related to nutritional status (MNA) (p = 0.001, B = -0.062). *Conclusion:* One in seven community-dwelling elderly with newly diagnosed AD is at risk of malnutrition. The degree of impairment in daily functioning is independently related to nutritional status. Therefore, assessment of the nutritional status should be included in the comprehensive assessment of AD patients. The relation between daily functioning, nutritional status and AD warrants further investigation.

Key words: Alzheimer's disease, community-dwelling, nutritional status, cross-sectional study.

Introduction

It is estimated that the number of people with dementia will double every 20 years. In this scenario, by 2020 about 40 million people will be affected by dementia worldwide (1). Alzheimer's Disease (AD) is the most frequent cause of dementia (1, 2). In 1907, Alois Alzheimer described weight loss in his first patient (3) and weight loss is currently recognized as a clinical feature of AD (4). Weight loss occurs in approximately 40% of AD patients and can present in all stages of the disease, even before the diagnosis has been made (5, 6).

Even though the exact mechanism of weight loss in AD patients has not been clarified (5), it has been shown that weight loss and malnutrition in AD patients are associated with several adverse outcomes such as progression of cognitive decline (5, 7-9), dependency (7-9), higher incidence of behavioural disorders (8), increased morbidity (5), decrease in quality of life of both the patient and his caregiver (5) and an increased mortality (10-12).

Weight loss is considered a characteristic of malnutrition (13). Although weight loss often occurs in AD patients and its association with adverse outcomes, little is known about the prevalence of malnutrition in community-dwelling AD patients, especially in newly diagnosed AD patients. Early detection of poor nutritional status, and its causes, is crucial for adequate intervention to prevent or diminish the adverse outcomes. The Mini Nutritional Assessment (MNA) is specifically developed and validated to identify malnutrition in older people (14-17).

This cross-sectional study was conducted in order to assess the prevalence of malnutrition, based on the MNA, and the relation of various factors to nutritional status in community-dwelling elderly with newly diagnosed AD.

Methods

Study design and setting

This retrospective cross-sectional study is based on data collected during 10 years (1998-2008) in AD patients seen at a memory clinic of a medium sized hospital in a rural part of the East of the Netherlands. Almost all patients were referred by a general practioner, sometimes they were referred by a specialist. At the time the diagnosis AD was made, socio-demographic characteristics and data on nutritional status, cognitive function, functional status and behaviour were assessed by the multidisciplinary team of the memory clinic.

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Participants

The study population consisted of 341 patients with newly diagnosed AD according to the criteria of the NINCDS-ADRDA (4), who lived at home or in residential care at the time the diagnosis AD was made. None of the patients used nutritional supplements. Patients aged 65 years or younger were excluded. Because this was a retrospective study, neither ethics committee approval nor informed consent were required.

Measurements

Cognitive functioning was assessed by the Mini Mental State Examination (MMSE) and the Cambridge Cognitive Examination (Camcog). The MMSE is a validated test, including 11 items reflecting different cognitive domains. Total MMSE score ranges from 0 to 30, a score of 24 or lower indicates disturbance of cognitive function (18). The Camcog consists of 67 questions to the patient. These questions cover multiple cognitive domains. Total Camcog score ranges from 0 to 107 where a score of 80 or lower is considered as having dementia. Generally, the lower the score, the more cognitive impairment (19).

Functional status was assessed by the Barthel Index (BI) and the Interview for Deterioration in Daily Living Activities in Dementia (IDDD). The BI measures the degree of impairment in Activities of Daily Living (ADL). It consists of 10 questions. The questionnaire is completed by the patient, family member or nurse. Total score ranges from 0 to 20, with the lower the score, the greater the impairment in ADL (20). The IDDD is specifically designed to assess functional changes in demented patients living at home. It consists of 33 questions for the caregiver of the patient. These questions focus on self care and, unlike the BI, to more complex activities (such as telephoning and writing). Total score ranges from 33 to 99, with the higher the score, the greater the impairment in daily functioning (21).

Behavioural functioning was assessed by the Revised Memory and Behaviour Problems Checklist (RMBPC). It consists of 25 questions for the caregiver. The questions involve the frequency of problematic behaviour in the patient and caregiver reactions to this behaviour. Total score ranges from 0 to 100 where the higher the score, the more behavioural problems (22).

Nutritional status was assessed by the Mini Nutritional Assessment (MNA) and the Body Mass Index (BMI). The MNA is a widely used tool for assessing the nutritional status of elderly. It is internationally well validated and has a high sensitivity, specificity and reliability. The MNA consists of 18 questions. Total MNA score ranges from 0 to 30, with the higher the score, the better the nutritional status. Depending on the total score, the patient is classified as well-nourished (MNA score >23.5), at risk of malnutrition (MNA score 17-23.5) or malnourished (MNA score <17) (14,15). BMI was calculated as weight/height^2. The BMI is a widely used and generally accepted measure of nutritional status. However, in the elderly the BMI should be interpreted with caution because of change in body composition. Moreover, there is no consensus on the appropriate cut-off value for malnutrition in the elderly (23).

Statistical Analysis

Data were analyzed with Statistical Package for the Social Sciences (SPSS) 16.0. Descriptive statistics are presented as means ± standard deviations for normally distributed continuous variables. For skewed distributed continuous variables, median and 25th – 75th percentiles are given. Number and proportion are given for categorical variables. We used the Kolmogorov Smirnov test to establish the distribution of the variable.

The MNA can be regarded as both a categorical variable with the subgroups 'well-nourished' (MNA score >23.5), 'at risk of malnutrition' (MNA score 17-23.5) or 'malnourished' (MNA score <17), as well as a continous variable. We were interested in the relation of various factors to the subgroups of the MNA (the MNA as categorical variable) and to the MNA as continous variable. Therefore, we assessed the relation between nutritional status (MNA) and socio-demographic characteristics (age and gender), cognitive function (MMSE, Camcog), functional status (BI, IDDD) and behaviour (RMBPC), in two ways. First, we compared the various factors between well-nourished AD patients (MNA score >23.5) and AD patients who were malnourished or at risk of malnutrition (MNA score ≤ 23.5). The independent sample t-test was performed to compare normally distributed continuous variables. We employed the Mann-Whitney U test to compare skewed distributed continuous variables. Fisher's exact test was used, because of its accuracy over the Pearson chi-square test (24), to compare categorical variables. Second, linear regression analysis was performed to assess the effect of various factors on nutritional status. The MNA was used as dependent variable. We first did an univariate linear regression analysis in order to determine which variables contributed substantially to the nutritional status. The variables that contributed substantially to the nutritional status (i.e. the significant variables from the univariate linear regression analysis, it involved: cognitive functioning (MMSE), basic daily functioning (BI) and basic and complex daily functioning (IDDD)), were then entered in the multivariate analysis by the forward-method, with a probability-or F-to-enter criterion <0.05. Only the IDDD met the probability-or F-to-enter criterion and was therefore the only independent variable that was entered in the multivariate linear regression analysis.

Hypotheses were two-tailed tested. A probability (p) value of less than 0.05 was considered significant.

Results

Patient characteristics and prevalence of malnutrition

Twenty-nine patients were excluded because of age, thus 312 patients were enrolled. Table 1 shows patient characteristics at the time the diagnosis AD was made. According to the MNA, the prevalence of malnutrition was 0% and 14.1% was at risk of malnutrition.

Table 1
Characteristics of the AD patients

Age (year)	n, mean ± SD	312, 77.6 ± 5.7
Women	n (%)	193 (61.9)
MNA (score)	n, median [25th-75th percentile]	312, 26.5 [25.0-27.5]
- well-nourished (MNA score: >23.5)	n (%)	268 (85.9)
- at risk of malnutrition (MNA score: 17-23.5)	n (%)	44 (14.1)
- malnourished (MNA score: < 17)	n (%)	0 (0.0)
BMI (kg/m²)	n, mean ± SD	312, 26.2 ± 4.4
MMSE (score)	n, mean ± SD	312, 20.6 ± 3.8
- MMSE ≤ 24	n (%)	271 (86.9)
Camcog (score)	n, mean ± SD	283, 67.0 ± 10.9
- Camcog ≤ 80	n (%)	260 (91.9)
BI (score)	n, median [25th-75th percentile]	312, 20.0 [19.0-20.0]
IDDD (score)	n, median [25th-75th percentile]	310, 40.0 [37.0- 44.0]
RMBPC (score)	n, mean ± SD	274, 29.0 ± 9.4

MNA = Mini Nutritional Assessment, BMI = Body Mass Index, MMSE = Mini Mental State Examination, Camcog = Cambridge Cognitive Examination, BI = Barthel Index, IDDD = Interview for Deterioration in Daily Living Activities, RMBPC = Revised Memory and Behaviour Problems Checklist

Table 2
Relation of various factors to nutritional status. Well-nourished AD patients versus AD patients at risk of malnutrition

		Well-nourished (MNA score >23.5)	**At risk of malnutrition (MNA score 17-23.5)**	**P**
Age (year)	n, mean ± SD	268, 77.5 ± 5.7	44, 78.2 ± 6.1	ns
Women	n (%)	169 (62.7)	24 (54.5)	ns
BMI (kg/m²)	n, median [25th-75th percentile]	268, 25.6 [23.8-28.4]	44, 23.4 [20.9-27.6]	0.001*
MMSE (score)	n, median [25th-75th percentile]	268, 21.0 [19.0-23.0]	44, 20.0 [18.0-23.0]	ns
- MMSE ≤ 24	n (%)	230 (85.8)	41 (93.2)	ns
Camcog (score)	n, mean ± SD	247, 67.0 ± 11.0	36, 67.0 ± 10.1	ns
- Camcog ≤ 80	n (%)	226 (84.3)	34 (77.3)	ns
BI (score)	n, median [25th-75th percentile]	268, 20.0 [19.0-20.0]	44, 20.0 [18.0-20.0]	ns
IDDD (score)	n, median [25th-75th percentile]	266, 40.0 [37.0-43.0]	44, 41.5 [38.3-48.0]	0.022*
RMBPC (score)	n, mean ± SD	235, 29.0 ± 9.6	39, 29.3 ± 8.4	

MNA = Mini Nutritional Assessment, BMI = Body Mass Index, MMSE = Mini Mental State Examination, Camcog = Cambridge; Cognitive Examination, BI = Barthel Index, IDDD = Interview for Deterioration in Daily Living Activities, RMBPC = Revised Memory and Behaviour Problems Checklist ; Age, Camcog, RMBPC: independent sample t-test. BMI, MMSE, BI, IDDD: Mann-Whitney U test; Gender, cut-off MMSE, cut-off Camcog, cut-off BI: Fischer's Exact test; * = significant ($p < 0.05$); ns = not significant;

Relation of various factors to nutritional status

Well-nourished AD patients (MNA >23.5) versus AD patients at risk of malnutrition (MNA 17-23.5)

Because no patient was malnourished, we compared well-nourished AD patients with AD patients at risk of malnutrition. Table 2 summarizes the differences between these groups. BMI was lower in AD patients at risk of malnutrition compared to well-nourished AD patients. AD patients at risk of malnutrition were more impaired in basic and complex daily functioning (IDDD) than well-nourished AD patients. No differences were found regarding age, gender, cognitive functioning (MMSE, Camcog), basic daily functioning (BI) and behavioral functioning (RMBPC).

Effect of various factors on nutritional status of AD patients

Table 3 presents the results of the univariate linear regression analysis. In univariate analysis, cognitive functioning (MMSE), basic daily functioning (BI) and basic and complex daily functioning (IDDD) were related to nutritional status (MNA). Only the IDDD met the probability-or F-to-enter criterion and was entered in the multivariate analysis. The degree of impairment in basic and complex daily functioning was independently related to nutritional status (IDDD, n = 310, R2 = 0.032, B = -0.062, β = -0.180, p = 0.001).

Table 3
Relation of various factors to nutritional status. Univariate linear regression analysis

	n	**R^2**	**B**	**β**	**p**
Age	312	0.001	-0.013	-0.033	ns
Gender	312	0.000	-0.034	-0.008	ns
MMSE	312	0.013	0.066	0.114	0.045*
Camcog	283	0.001	0.007	0.034	ns
BI	312	0.026	0.242	0.163	0.004*
IDDD	310	0.032	-0.062	-0.180	0.001*
RMBPC	274	0.002	0.010	0.042	ns

MMSE = Mini Mental State Examination, Camcog = Cambridge Cognitive Examination, BI = Barthel Index, IDDD = Interview for Deterioration in Daily Living Activities, RMBPC = Revised Memory and Behaviour Problems Checklist; R2 = represents the amount of variance in the dependent variable, explained by the independent variable; B = partial regression coefficient; β = standardized coefficient; * = significant ($p < 0.05$); ns = not significant

Discussion

Prevalence of malnutrition

To our knowledge, this is the first study in which nutritional status of newly-diagnosed AD patients was investigated. Nine other studies investigated the prevalence of malnutrition in community-dwelling AD patients. Six of them were performed in France (8, 9, 25-28), two in Italy (29, 30) and one in the Netherlands (31).

In the present study, the prevalence of malnutrition was 0% and 14.1% was at risk of malnutrition. We were surprised about these results, because these rates are considerably lower than rates found in the before mentioned studies, with prevalences of at risk of malnutrition (MNA ≤ 23.5) ranging from 26% to 80% (9, 25-31). Our results are most consistent with a French study of Guerin et al (8). In this study in 561 community-dwelling AD patients, the prevalence of malnutrition was 3% and 18% was at risk of malnutrition according to the MNA (8). The differences in prevalence might reflect differences in disease duration, which varied from 1 year (8, 26, 27, 30) to 5 years (25, 28). The risk of weight loss tends to increase with severity and progression of AD (12, 28). In addition, the differences may be explained by variations in size and characteristics of the study populations. For example, in one of the French studies, MMSE score was lower compared to our study population (24). More severe cognitive impairment increases the risk of malnutrition (16, 32, 33). However, the studies are quite similar regarding other characteristics such as BMI, age, gender, functional status and behavioural functioning. There could be other factors that may explain the differences in prevalence, such as geographic position. Our study was performed in a rural part of the East of the Netherlands. It could be that patients originating from this area have an eating pattern which results in a better nutritional status. Research into this would be interesting because this may provide new targets for the prevention and treatment of malnutrition. Because this was a single centre study, bias due to a systematic measurement error in rating nutritional status can not be ruled out. This could also have contributed to the low prevalence of (risk of) malnutrition

Relation of various factors to nutritional status

The degree of impairment in basic and complex daily functioning, operationalized with the IDDD, was independently related to nutritional status. In addition, AD patients at risk of malnutrition were more impaired in basic and complex daily functioning than well-nourished AD patients. These results suggest a relation between nutritional status and basic and complex daily functioning in AD patients. Several studies have confirmed this relation (8, 9, 30).

We hypothesise that there is a mutual relation between nutritional status and daily functioning, in which on the one hand functional decline worsens nutritional status and on the other hand malnutrition worsens functional status. How could this mutual relation be explained? It has been hypothesized that decreased energy intake, secondary to functional impairment associated with eating, contributes to weight loss in AD patients (34). This could explain how functional decline worsens nutritional status. The assumption that functional decline may be a consequence of malnutrition could be explained as follows: several nutrients effect cognition by affecting multiple brain processes such as neurotransmitter pathways and synaptic transmission (35). Cognition, in turn, strongly influences daily functioning of AD patients (36). It could be that, through a deficiency of nutrients in malnourished AD patients, brain processes will be disrupted which results in an increase in cognitive impairment and hence impairment in daily functioning. This is supported by the finding that a multi-nutrient drink improved BMI, memory and daily functioning of AD patients (37). Studies of individual cognitive domains showed that executive functioning, memory and visual perception predict daily functioning of AD patients (38, 39). Studies on the relation of nutritional status to daily functioning, executive functioning, memory, visual perception and brain areas underlying these functions are necessary in order to clarify the mechanism that underlies the relation between nutritional status and daily functioning. A better understanding of this mechanism is relevant since it could result in new disease-modifying interventions.

Cognitive functioning was not independently related to nutritional status in this study. Therefore, the assumption that functional decline may be a consequence of malnutrition could also be explained by mechanisms in which cognition plays no role, such as sarcopenia. Inadequate nutrition is considered a mechanism of sarcopenia, which in turn is associated with impaired ability to perform activities of daily living (40).

In sum, there is probably a mutual relation between nutritional status and daily functioning in AD patients. Although the mechanism that underlies this relation has not been clarified, we emphasize that: 1. health care providers should be attentive to the nutritional status of AD patients with increasing care dependency and 2. nutritional support of malnourished AD patients may perhaps lead to longer maintenance of independence. A study among hospital-admitted malnourished elderly showed benefit of energy and protein enriched nutritional support on functional limitations (41). Future prospective randomized controlled trials on the effect of nutritional support in community-dwelling AD patients are needed to confirm these findings, especially because the treatment options in AD are still limited

Strengths and limitations

The major strength of the present study is that nutritional status was evaluated in a large population of community-dwelling patients with newly diagnosed AD by using the full MNA. The focus on newly diagnosed AD patients allows the outline of preventive actions already at the diagnostic stage of AD patients. However, some limitations of the study must be considered when interpreting the findings. The findings do not reflect patients with a longer disease duration, therefore the generalization of the findings is restricted. In addition, since

none of the patients was malnourished, it was not possible to compare well-nourished patients with malnourished patients. Since this was a retrospective study, we were dependent on data collected in the past. Hence, we could not account for all known factors associated with weight loss, such as comorbidity (13, 42), use of medication (42) and caregiver burden, which is mentioned a risk factor for weight loss in community-dwelling AD patients (43). As this study was not longitudinal, it was not possible to attribute cause and effect relations. Moreover, because this was a single centre study, bias due to a systematic measurement error can not be ruled out. Another limitation concerns that data was collected over a 10 year period. Within this timeframe, the characteristics of the 'AD patient' could have changed.

Conclusion

In this study, one in seven community-dwelling elderly with newly diagnosed AD is at risk of malnutrition. The degree of impairment in daily functioning is independently related to nutritional status. Therefore, assessment of the nutritional status should be included in the comprehensive assessment of AD patients. The relation between daily functioning, nutritional status and AD warrants further investigation.

Conflicts of interest: C.J.M. Schölzel-Dorenbos, J.H.M. van Steijn, P.E. van Walderveen, C.S. van der Hooft and E. Droogsma declare no conflict of interest. D.Z.B. van Asselt is member of the advisory board of Janssen Pharma and Nutricia.

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