



Awareness of Diagnosis in Persons with Early-Stage Alzheimer's Disease: An Observational Study in Spain

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ABSTRACT

Introduction: Limited information is available on people's experiences of living with Alzheimer's disease (AD) at earlier stages. This study

assessed awareness of diagnosis among people with early-stage AD and its impact on different person-centered outcome measures.

Methods: We conducted an observational, cross-sectional study in 21 memory clinics in

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Spain. Persons aged 50–90 years, diagnosed with prodromal or mild AD (NIA/AA criteria), a Mini Mental State Examination (MMSE) score ≥ 22 , and a Clinical Dementia Rating-Global score (CDR-GS) of 0.5 or 1.0 were recruited. The Representations and Adjustment to Dementia Index (RADIX) was used to assess participants' beliefs about their condition and its consequences.

Results: A total of 149 persons with early-stage AD were studied. Mean (SD) age was 72.3 (7.0) years and 50.3% were female. Mean duration of AD was 1.4 (1.8) years. Mean MMSE score was 24.6 (2.1) and 87.2% had a CDR-GS score of 0.5. Most participants ($n = 84$, 57.5%) used a descriptive term related to specific AD symptoms (e.g., memory difficulties) when asked what they called their condition. Participants aware of their diagnosis using the term AD ($n = 66$, 45.2%) were younger, had more depressive symptoms, and poorer life satisfaction and quality of life compared to those without awareness of their specific diagnosis. Practical and emotional consequences RADIX scores showed a significant negative correlation with Quality of Life in Alzheimer's Disease score ($\rho = -0.389$ and -0.413 , respectively; $p < 0.0001$). Years of education was the only predictor of awareness of AD diagnosis [OR = 1.04 (95% CI 1.00–1.08); $p = 0.029$].

Conclusions: Awareness of diagnosis was a common phenomenon in persons with early-stage AD negatively impacting their quality of life. Understanding illness representations in earlier stages may facilitate implementing optimized care that supports improved quality of life and well-being.

Keywords: Alzheimer's disease; Awareness; Illness representation; Well-being; Quality of life; Diagnosis

Key Summary Points

Awareness of the condition and its diagnosis among persons with early-stage Alzheimer's disease has been little explored.

Awareness of Alzheimer's disease diagnosis was a common phenomenon in persons in early stages negatively impacting their quality of life.

The identification of persons with awareness of their diagnosis, especially in the early stages of the disease, should be a goal to implement individualized strategies to preserve quality of life.

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INTRODUCTION

Alzheimer's disease (AD) is the most common type of dementia and its prevalence continues to increase mainly because of population growth and ageing [1]. Impaired awareness of cognitive and functional deficits or anosognosia is a common phenomenon in persons with AD with a prevalence ranging from 21% to 81% [2, 3]. Low awareness predicts progression to dementia in both subjects with normal cognition and persons with mild cognitive impairment by an average of 3 years [4, 5].

The impact of anosognosia on AD persons and their caregivers has been extensively studied, but awareness of the condition and its diagnosis has only recently begun to be explored [2, 3, 6–12]. Quinn et al. developed the Representations and Adjustment to Dementia Index (RADIX), a specific instrument to assess people's beliefs about dementia and their impact on subsequent adjustment [13]. In a sample of 917 persons with mild-to-moderate dementia in the UK, those with awareness of their condition reported a higher rate of depression and lower indices of well-being and psychological resources [12].

AD care should focus on person-centered outcomes [14, 15]. Maintaining autonomy and quality of life based on persons' preferences and beliefs is essential, especially in the early stage of the disease when decision-making capacity is less impaired [14–16]. The aim of this study was to assess awareness of diagnosis among persons with early-stage AD and its impact on different psychological and behavioral dimensions.

METHODS

This is an observational, cross-sectional study conducted at 21 hospital-based memory clinics. Key eligibility criteria included age between 50 and 90 years old, a diagnosis of prodromal or mild AD (National Institute on Aging/Alzheimer's Association criteria), a Mini Mental State Examination (MMSE) score ≥ 22 , and a Clinical Dementia Rating-Global score (CDR-GS) of 0.5 or 1.0 [17, 18]. Participants were consecutively recruited in the context of their regular follow-

up visits between February and June 2021. This study was approved by the research review board of Hospital de la Santa Creu i Sant Pau, Barcelona, Spain (reference number EC/20/396/6186 [OBS]), and performed in accordance with the 1964 Helsinki Declaration and its later amendments. According to Spanish legislation (Orden SAS/3470/2009), non-interventional studies require approval by a single ethics committee and this approval applies to all participating centers. All participants provided written informed consent.

Outcome Measures

The RADIX is a brief, self-report instrument validated in people with mild to moderate dementia to assess their understanding of the condition and its consequences in five components: identity, cause, disease course over time (timeline), possibilities for controlling the disease, and practical and emotional consequences [13]. A nine-question screening checklist is included to screen out those who did not identify any difficulties or changes. Identity and cause are open questions to capture the perspective of the person with dementia. A list of options of possible causes is offered to the respondent including ageing, changes within the brain, disease or physical condition, hereditary condition, lifestyle events, or don't know. Questions on timeline and control are single items rated on a four-point scale. For practical and emotional consequences, responses to the questions are rated on a four-point scale (from strongly disagree to strongly agree) and can be summed to give an overall score and then divided by 4 and 5 to give the mean score, respectively. Higher scores indicate greater negative consequences. This questionnaire was developed in English and is available at <https://medicine.exeter.ac.uk/reach/publications/>. In this study, a Spanish version was used after previous forward/backward translations.

The Quality of Life in Alzheimer's Disease (QoL-AD), Functional Activities Questionnaire (FAQ), Beck Depression Inventory-Fast Screen (BDI-FS), Beck Hopelessness Scale (BHS), Satisfaction With Life Scale (SWLS), and General

Self-Efficacy Scale (GSES) were used to gather information on quality of life, functioning, mood, feelings of hopelessness, life satisfaction, and self-efficacy, respectively [19–24]. Cognition was assessed using the Alzheimer Disease Assessment Scale-Cognitive (ADAS-Cog13) [25]. The QoL-AD is a 13-item self-report questionnaire designed to assess quality of life of persons with a diagnosis of AD [19]. Each item is rated using a four-point scale ranging from 1 (poor) to 4 (excellent). Higher scores indicate better quality of life. The FAQ is a 10-item, informant-based instrument to measure activities of daily living in elderly people [20]. Each item is rated using a four-point scale ranging from 0 (normal) to 3 (dependent). A cutoff ≥ 6 indicates functional impairment. The BDI-FS is self-report seven-item questionnaire assessed on a four-point scale (no symptoms to severe symptoms) [21]. Total score ranges from 0 to 21 with a cutoff ≥ 4 indicating the presence of depressive symptoms. The BHS is a 20-item self-report inventory to measure three major components of hopelessness: feelings about the future, loss of motivation, and future expectations [22]. Each optimistic response is scored as 0 and each pessimistic response is scored as 1. Total score ranges from 0 to 20 with higher values indicating higher levels of hopelessness. A cutoff ≥ 9 indicates moderate-to-severe hopelessness and identifies a high-risk group for potential suicide [26]. Participants indicated how much they agree or disagree with each of the five items of the SWLS using a seven-point scale that ranges from 1 (strongly disagree) to 7 (strongly agree) [23]. A cutoff score ≥ 25 indicates that respondents are satisfied or extremely satisfied with their life. The GSES is a 10-item self-report instrument to assess whether a person believes he or she can perform novel or difficult tasks or cope with adversity in different domains of functioning [24]. Each item is rated using a four-point scale ranging from 1 (not at all true) to 4 (exactly true). Higher scores indicate higher levels of an optimistic self-belief.

Definitions

Awareness of diagnosis was defined when participants used a diagnostic term or descriptive terms with specific symptoms to refer to the diagnosis of their illness (RADIX diagnosis item) [13]. Awareness of AD diagnosis was defined when participants specifically used the word Alzheimer to refer to the diagnosis of their condition. Participants who were able to give the diagnosis using the term AD and considered that their condition was going to worsen over time were classified as high awareness group (RADIX diagnosis and timeline items) [12, 13].

Statistical Analysis

Logistic regression was used to explore predictors of AD awareness using sociodemographic, clinical, cognitive, and psychological/behavioral characteristics. Variables with a statistical relationship to awareness and a p value of less than 0.2 were candidates for the model. Stepwise automatic variable selection method was applied in model building. Correlations between RADIX components and quality of life were also analyzed.

RESULTS

A total of 149 persons with early-stage AD were studied. Mean (SD) age was 72.3 (7.0) years and 50.3% were female. Mean duration of AD was 1.4 (1.8) years. Mean MMSE score was 24.6 (2.1) and 87.2% had a CDR-GS score of 0.5. Sociodemographic and clinical characteristics are shown in Table 1.

Only three persons (2%) did not complete any of the RADIX screening items. Most participants ($n = 84$, 57.5%) used a descriptive term related to specific AD symptoms (e.g., memory difficulties) when asked what they called their condition. Don't know (22.7%), ageing (21.4%), brain changes (20.7%), and hereditary condition (15.6%) were the most common reported causes. Illness representations according to RADIX responses are shown in Table 2.

Table 1 Sociodemographic and clinical characteristics of the participants

| | <i>N</i> = 149 |
|--|----------------|
| Age, years, mean (SD) | 72.3 (7.0) |
| Sex, female, <i>n</i> (%) | 75 (50.3) |
| Years of education, mean (SD) | 13.1 (9.9) |
| Time since diagnosis, years, mean (SD) | 1.4 (1.8) |
| CDR-GS score of 0.5, <i>n</i> (%) | 130 (87.2) |
| MMSE score, mean (SD) | 24.6 (2.1) |
| ADAS-Cog13 score, mean (SD) | 24.4 (5.2) |
| QoL-AD score, mean (SD) | 37.9 (4.5) |
| FAQ score, mean (SD) | 5.9 (6.2) |
| FAQ score \geq 6, <i>n</i> (%) | 57 (38.2) |
| SWLS score, mean (SD) | 27.5 (5.7) |
| SWLS score \geq 25, <i>n</i> (%) | 120 (80.5) |
| GSES score, mean (SD) | 29.9 (6.3) |
| BDI-FS score, mean (SD) | 2.1 (2.2) |
| BDI-FS score \geq 4, <i>n</i> (%) | 33 (22.1) |
| BHS score, mean (SD) | 10.7 (2.4) |
| BHS score \geq 9, <i>n</i> (%) | 124 (83.2) |

ADAS-Cog Alzheimer Disease Assessment Scale-Cognitive, *BDI-FS* Beck Depression-Fast Screen, *BHS* Beck Hopelessness Scale, *CDR-GS* Clinical Dementia Rating-Global Score, *FAQ* Functional Activities Questionnaire, *GSES* Global Self-Efficacy Scale, *MMSE* Mini Mental State Examination, *QoL-AD* Quality of Life in Alzheimer's Disease, *SD* standard deviation, *SWLS* Satisfaction With Life Scale

In total 116 (79.4%) participants were aware of their condition (Table 2) and 66 (45.2%) used the term AD when asked if they knew their specific diagnosis (Table 3). These persons were younger, had more depressive symptoms, and poorer life satisfaction and quality of life compared to those without awareness of their specific diagnosis (Table 3).

Nineteen (13%) participants were able to give the AD diagnosis and considered that their condition was going to worsen over time. A

Table 2 Illness representations according to RADIX responses (*N* = 146)

| Categories | <i>N</i> (%) |
|--|--------------|
| Identity | |
| Descriptive term using specific symptoms | 84 (57.5) |
| Diagnostic term | 46 (31.5) |
| Don't know | 10 (6.8) |
| Unclassifiable | 6 (4.1) |
| Diagnosis | |
| Diagnostic term | 83 (45.2) |
| Descriptive term using specific symptoms | 33 (22.6) |
| Don't know | 27 (18.5) |
| Unclassifiable | 3 (2.0) |
| Cause | |
| Don't know | 35 (22.7) |
| Ageing | 33 (21.4) |
| Brain changes | 32 (20.7) |
| Hereditary | 24 (15.6) |
| Lifestyle | 18 (11.7) |
| Illness or physical problem | 5 (3.2) |
| Unclassifiable | 7 (4.5) |
| Evolution | |
| Get worse | 71 (48.6) |
| Stay the same as it is now | 31 (21.2) |
| Get better | 26 (17.8) |
| Don't know | 18 (12.3) |
| Practical consequences, mean (SD) | 1.8 (0.6) |
| Emotional consequences, mean (SD) | 2.2 (0.8) |

RADIX Representations and Adjustment to Dementia Index, *SD* standard deviation

logistic regression approach was used to explore predictors of awareness among these participants. Years of education was the only predictor of high awareness of AD diagnosis [OR = 1.04 (95% CI 1.00–1.08); *p* = 0.02] (Table 4).

Table 3 Description of participants according to awareness of AD diagnosis

| | AD awareness <i>N</i> = 66 | No AD awareness <i>N</i> = 80 | <i>p</i> value |
|---|-------------------------------|----------------------------------|----------------|
| Age, years, mean (SD) | 70.2 (6.6) | 73.8 (6.9) | 0.001 |
| Sex, female, <i>n</i> (%) | 34 (51.5) | 40 (50.0) | 0.869 |
| Years of education, mean (SD) | 13.9 (11.5) | 12.6 (8.5) | 0.446 |
| Disease duration, years, mean (SD) | 1.3 (1.8) | 1.3 (1.6) | 0.861 |
| CDR-GS score of 0.5, <i>n</i> (%) | 61 (92.4) | 67 (83.7) | 0.134 |
| MMSE score, mean (SD) | 24.8 (2.2) | 24.5 (2.0) | 0.369 |
| ADAS-Cog13 score, mean (SD) | 24.2 (5.8) | 24.4 (4.8) | 0.792 |
| QoL-AD score, mean (SD) | 36.6 (4.5) | 38.8 (4.1) | 0.002 |
| FAQ score, mean (SD) | 4.9 (5.1) | 6.5 (5.0) | 0.104 |
| SWLS score, mean (SD) | 26.4 (6.3) | 28.6 (4.9) | 0.015 |
| GSES score, mean (SD) | 29.5 (6.3) | 30.6 (6.3) | 0.307 |
| BDI-FS score, mean (SD) | 2.7 (2.6) | 1.5 (1.7) | 0.001 |
| BDI-FS score ≥ 4 , <i>n</i> (%) | 22 (33.3) | 11 (13.7) | 0.009 |
| BHS score, mean (SD) | 11.1 (2.7) | 10.4 (2.2) | 0.086 |
| Emotional consequences score, mean (SD) | 2.4 (0.8) | 2.0 (0.7) | 0.003 |

Table 3 continued

| | AD awareness <i>N</i> = 66 | No AD awareness <i>N</i> = 80 | <i>p</i> value |
|---|-------------------------------|----------------------------------|----------------|
| Practical consequences score, mean (SD) | 1.9 (0.6) | 1.7 (0.6) | 0.037 |

AD Alzheimer's disease, *ADAS-Cog* Alzheimer's Disease Assessment Scale-Cognitive, *BDI-FS* Beck Depression-Fast Screen, *BHS* Beck Hopelessness Scale, *CDR-GS* Clinical Dementia Rating-Global Score, *FAQ* Functional Activities Questionnaire, *GSES* Global Self-Efficacy Scale, *MMSE* Mini Mental State Examination, *QoL-AD* Quality of Life in Alzheimer's Disease, *SD* standard deviation, *SWLS* Satisfaction With Life Scale

Practical and emotional consequences RADIX scores showed a significant negative correlation with QoL-AD score ($\rho = -0.389$ and -0.413 , respectively; $p < 0.0001$).

DISCUSSION

The impact of impaired awareness on persons with AD and their caregivers has been extensively studied [2, 6–8, 27, 28]. Anosognosia was associated with poor autonomy, greater frequency and severity of behavioral symptoms, lower treatment adherence, greater caregiver

Table 4 Predictors of awareness using logistic regression analysis

| | OR | 95% CI | <i>p</i> value |
|-----------------------|------|-----------|----------------|
| Age | 0.94 | 0.88–1.01 | 0.103 |
| Years of education | 1.04 | 1.00–1.08 | 0.029 |
| BDI-FS score | 1.14 | 0.95–1.38 | 0.156 |
| BDI-FS score ≥ 4 | 2.26 | 0.81–6.32 | 0.118 |

BDI-FS Beck Depression-Fast Screen, *CI* confidence interval, *OR* odds ratio

burden, and discrepancy in perception of quality of life between people with AD and their caregivers [2, 27, 28].

Different studies have shown that persons with AD are still able to describe their problems, experiences, and preferences at different stages of the disease [10, 14, 15]. In a qualitative and quantitative study with mild and moderate AD persons, Trindade et al. found that awareness of condition was more preserved than awareness of specific functional deficits [10]. Mayelle et al. using the Awareness of Self and Disease Assessment scale found that awareness in AD is heterogeneous and can fluctuate over time with three different patterns (deficit, stability, or improvement) [11]. However, little is known about the impact of having awareness of diagnosis, especially at earlier stages of the disease.

In our study, awareness of diagnosis was a common phenomenon with 45% of persons being able to use the term AD in a population with a mean disease duration of 1.4 years. Awareness was associated with the presence of depressive symptoms, poor life satisfaction, and quality of life.

Similar findings were found in a recent systematic review in persons with mild to moderate AD by Azocar et al. [28]. Most studies showed a negative association between impaired awareness and depression and anxiety (Pearson correlations ranging from 0.3 to 0.7). The IDEAL (Improving the experience of Dementia and Enhancing Active Life) study investigated illness representations using the RADIX questionnaire in a population with mild-to-moderate dementia in the UK [12]. The participants (11.2%) categorized by high awareness of their dementia diagnosis and knowledge of its causes and prognosis reported a higher rate of depressive symptoms and lower satisfaction with life, optimism, self-efficacy and self-esteem [12]. Younger age and depressed mood were stronger predictors of this awareness group than the level of cognitive or functional impairment [12]. In our study, the only predictor of awareness of AD was years of education.

Persons' beliefs and expectations about an illness determine their emotional reactions and coping responses [29]. Persons prefer to be

informed about their AD diagnosis, which has been associated with a better quality of life [15, 30]. However, having a better awareness of AD diagnosis correlates with more depressive symptoms and poorer quality of life [12]. In our study, a negative hope for the future, one of the most important factors for suicide, was also highly prevalent [26]. Therefore, identifying and understanding persons' representations of AD from the onset of the disease may be essential for early implementation of individualized interventions to enable well-being and maintenance of independence where possible.

Our study has some limitations that deserve mention. First, the aim of this study was to assess awareness of condition and its associated factors using a comprehensive battery of self-report measurements. Traditionally, self-report measures have been considered insensitive in this disease [31]. The discrepancy between persons' and caregivers' scores on quality of life and other symptom dimensions begins even with very mild cognitive impairment. Second, although the RADIX is a useful and validated tool to understand dementia representations, the use of open questions and the listing of options for possible causes in this questionnaire can be challenging for respondents and the reliability of their subjective assessments [12, 13]. Third, given the cross-sectional design of the study, we have no information about participants' potential changes in their levels of awareness over time [9, 11]. Finally, this study did not collect whether the participants had received any information on the disease and its long-term prognosis. Therefore, we cannot rule out that a greater awareness of the diagnosis may reflect a better provision of information.

CONCLUSIONS

Awareness of diagnosis was a common phenomenon in persons with early-stage AD and negatively impacted their quality of life and well-being. Awareness of diagnosis could be a signal to identify early in order to implement specific strategies to prevent depression and preserve quality of life. The approach to such actions must be based on a holistic view of the

person and their environment and must be treated in a multidisciplinary way.

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Compliance with Ethics Guidelines. This study was approved by the research review board of Hospital de la Santa Creu i Sant Pau, Barcelona, Spain (reference number EC/20/396/6186 [OBS]), and performed in accordance with the 1964 Helsinki Declaration and its later amendments. According to Spanish legislation (Orden SAS/3470/2009), non-interventional studies require approval by a single ethics committee and this approval applies to all participating centers. Participants provided written informed consent.

Data Availability. Qualified researchers may request access to individual patient-level data through the corresponding author. The datasets generated during the analysis of the study are available from the corresponding author on reasonable request.

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