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Research Report

Measures of Awareness in Alzheimer's Disease and Clinical Differences Between Groups with Preserved, Impaired, and Absent Awareness

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Abstract.
Background: Awareness is a heterogeneous construct that requires accurate assessment. There is no consensus on the best methodology for capturing the phenomenon, thus leading to inconsistent results in this area.
Objective: We aim to evaluate the reliability of clinicians' ratings and a discrepancy assessment method, examining groups of people with Alzheimer's disease (PwAD) according to their degree of awareness and demographic and clinical aspects.
Methods: We cross-sectionally assessed 134 PwAD and their caregivers. Individuals' level of awareness was assessed with two methods: clinicians' ratings identified three groups (preserved awareness, impaired awareness, and absent awareness), while discrepancy assessment identified four groups (preserved awareness, mildly impaired awareness, moderately impaired awareness, and absent awareness).
Results: Clinicians' ratings showed significant differences between PwAD with preserved, impaired, and absent awareness groups in cognition, functionality, and neuropsychiatric symptoms. There was a significant difference in caregivers' anxiety between the impaired and absent awareness groups. Discrepancy assessment showed no clinical differences between the preserved and mildly impaired awareness groups or between the absent and moderately impaired awareness groups. A significant difference in functionality was observed between the other groups.
Conclusions: Clinical aspects of each measure tended to differ between the chosen methods. Impairments in awareness fluctuate despite disease progression. Cognition and severity of disease cannot explain deficits in awareness.

Keywords: Alzheimer's disease, awareness, dementia, measures

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INTRODUCTION

Many empirical studies exploring Alzheimer's disease (AD) have focused on comprehending the awareness phenomenon. Awareness is the person's ability to recognize changes and deficits associated with a disease process [1]. Awareness includes three stages: the competence to monitor immediate functioning, the ability to judge performance in a specific domain, and the ability to weigh the nature and impact of a disease or health condition [2].

Nevertheless, the heterogeneity and lack of clear definitions make it difficult to achieve consistent results in this area [3–7]. Therefore, when studying awareness, it is essential to acknowledge the concept chosen in the research, the measure selected to capture the phenomenon, and the specific domain of awareness studied [4]. Since awareness is a relational and heterogeneous construct, the degree of impairment varies between people with Alzheimer's disease (PwAD), ranging from preserved and mildly impaired awareness to a complete unawareness of the deficit. Awareness also differs between domains [3, 8], so PwAD can be aware of some specific deficits or domains but not others.

Deficits in awareness are expected to get worse over time. However, longitudinal studies have reported that awareness can either become exacerbated, remain stable, or even improve, when PwAD present better awareness of their deficits [9, 10]. Consequently, deficits in awareness may not be related only to the severity of cognitive impairment. While some studies indicate an association between awareness and disease severity, others question this relationship, highlighting that awareness is a nonlinear phenomenon [3, 11], such that it does not directly mirror disease progression. Even PwAD with moderate dementia can be aware of their deficits, while others with mild dementia do not notice them. Clinical aspects and demographic characteristics such as fewer signs of depression, deficits in functional activities, greater dementia severity, older age, poor socioeconomic status, and lower education have been related to the impairment in awareness [2, 10, 12, 13].

In addition, some studies discuss the relationship between awareness and ethical and legal issues in PwAD [14]. Appelbaum and Grisso [15] allude to four decision-making capacities: communicating consistently, understanding choices, evaluating implications and consequences, and reasoned estimates of risks and benefits. A recent study [16] showed that decision-making capacity is related to the cognitive and functional domains of awareness and is relatively independent of the emotional functioning and relationship domains. PwAD who are unaware of their disease or of their cognitive and functional impairments may be unlikely to appreciate the personal benefits of an alternative or to accurately understand and judge the consequences of a decision. Importantly, the dementia diagnosis and the stigma involving generalization of deficits in awareness in PwAD have significant implications for their autonomy and independence [17].

To access deficits in awareness in dementia, different methods have been developed that vary in content and form, reflecting the researchers' different conceptions of awareness [3]. A recurrent finding in clinical practice involves impairment in the awareness of cognitive deficits and behavioral changes; however, the diagnosis of deficits in awareness is frequently made subjectively or with non-standardized methods [18].

The most common procedures used to assess awareness in PwAD are (1) clinicians' ratings, (2) the discrepancy between self-report by PwAD and caregiver information, and (3) the comparison between self-report by PwAD and their performance on a given task [18, 19]. It is important to note that each methodology elicits and measures distinct aspects of awareness [20], since awareness is a relational concept, as stated above. The diversity of instruments used to evaluate awareness and its different domains and definitions help explain the wide variation of the prevalence of deficits in awareness in AD, ranging from 20% to 81% [11, 12].

Regarding the different methodologies used, clinicians' ratings are broadly applied, usually based on a routine interview and with a subjective perspective [18, 19, 21, 22]. A structured scale is not used for this assessment, which hinders or even precludes replication. In addition, clinicians' ratings may fail to capture the non-linearity and multidimensionality of awareness, grasping it as a symptom of the disease process limited to a dichotomous construct [21].

Prediction-performance assessment has limitations involving a person's judgment of their performance in a particular neuropsychological task. For example, some scales feature psychometric data with good validity to assess performance in a specific function, but this can result in overlooking deficits in other areas [19]. A person may thus be aware of one domain such as memory, but not others.

Questionnaire-based assessment features the calculation of discrepancy scores between patient and informant ratings. The informant is usually a relative or family caregiver. Although discrepant methods have received some criticism, such as the influence of caregiver burden, depression, and other emotional or cognitive conditions in their evaluation [18, 19], they may be an essential source of information on the routines and deficits of PwAD [23].

Only a few studies have explored different methods for evaluating awareness. Correlations have been found between clinicians' ratings and the discrepancy questionnaire, whereas prediction performance showed no relationship to other forms of assessment [20, 24]. Moreover, the research has not investigated the relationship between the methods used and clinical aspects of the disease. Awareness in AD has multiple causes, and the method used to elicit this phenomenon is influenced by these factors [24].

It is essential to develop a reliable and meaningful strategy to identify and assess deficits in awareness. Realizing that the nonexistence of an accepted gold standard method results from the diverse approaches in awareness evaluation [19], we aimed to evaluate the reliability of clinicians' ratings and a discrepancy assessment method, the Assessment Scale of Psychosocial Impact of the Diagnosis of Dementia (ASPIDD), which is a validated instrument to assess awareness in dementia, with good to excellent internal consistency ($\alpha = 0.87$) [1]. The ASPIDD is a discrepant instrument encompassing PwAD and caregiver reports in a multidimensional evaluation that includes four domains scored independently or globally: cognitive deficits and health conditions, emotional state, social functioning and relationships, and functional impairments [1]. We thus examined groups of PwAD according to their degree of awareness, using both clinicians' ratings and ASPIDD scores to demarcate the groups. We investigated the groups' demographic characteristics and clinical aspects to better understand the assessments of awareness patterns and discrepancies. Our working hypothesis was that clinicians' ratings may not cover the heterogeneity of awareness, thus decreasing the sensitivity of awareness measurement. Moreover, we expected that when clinicians assess deficits in awareness, their assessment will relate more to cognition and disease severity since the assessment is based on a clinical interview. Conversely, the ASPIDD score will report more association with functionality than with cognition.

METHODS

Design

The study adopted a cross-sectional design.

Participants

Participants ($n = 134$) were recruited from the Center for Alzheimer's Disease of the Universidade Federal do Rio de Janeiro (UFRJ). Inclusion criteria were diagnosis of possible or probable AD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders 5th edition [25], a score of 11 or above on the Mini-Mental State Examination (MMSE) [26], and mild or moderate dementia according to the Clinical Dementia Rating (CDR) [27]. We excluded PwAD with aphasia, head trauma, history of alcohol abuse, or epilepsy.

Caregivers were selected as the main individuals responsible for caring for the PwAD (i.e., family members such as sons/daughters, wives/husbands, brothers/sisters, and grandchildren). They were excluded if they reported a history of their own psychiatric or cognitive disorders. Caregivers needed at least a weekly face-to-face meeting with PwAD to provide detailed information about their routine.

Ethical approval was provided by the Institutional Review Board of the Institute of Psychiatry (IPUB) at the Universidade Federal do Rio de Janeiro (UFRJ), and all participants gave informed consent.

Procedure

The PwAD underwent assessments of their cognition and the awareness of their diseases. Caregivers provided information on the respective individuals with AD (including demographics, functionality, dementia severity, awareness of disease, and neuropsychiatric and depressive symptoms) and underwent a burden assessment and mood questionnaires. Duration of the illness was based on the onset of symptoms, i.e., complaints related to memory and reported by the patients and caregivers at the beginning of treatment, as described in the patient files. Caregivers and PwAD were interviewed separately.

Measures

Sociodemographic characteristics of PwAD and caregivers (age, gender, marital status, education, and family relations) were recorded.

Table 1 describes the instruments.

Table 1
Instruments

People with AD	
Cognitive status	Cognitive level was measured with MMSE, a cognitive screening test that evaluates orientation, memory, attention, and ability to name and follow verbal and written commands. The total score ranges from zero to 30. Lower scores indicate impaired cognition [26]. ADAS-cog assesses the intensity of cognitive changes. The cognitive subscale includes items 1-11, with a maximum score of 70. The cognitive domains evaluated are memory, language, praxis, and command understanding. Higher scores indicate worse performance [28].
Dementia severity	Severity of dementia was measured by the CDR, with stages ranging from zero (no dementia) to 3 (severe dementia) according to impairments in cognition, behavior, and ADL [27].
Depressive symptoms	The CSDD assesses mood and physical symptoms, circadian functions, and behavioral indicators related to depression in dementia. Scores above 13 indicate presence of depression [29].
Functional measurement	The PFAQ is a caregiver-reported inventory that evaluates basic and instrumental ADL. The ratings for each item range from average (0) to dependent (3), totaling 30 points. Higher scores indicate lower functional status [30].
Neuropsychiatric symptoms	The NPI evaluates the presence of delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, motor disorders, sleep disorders, and eating abnormalities. The NPI score is the sum of frequency versus severity ratings for all symptoms. The frequency is rated from one (absent) to four (frequently), and intensity from one (mild) to three (severe). The total score can range from zero to 144 points [31].
Caregiver's measurements	
Burden	Caregiver burden was assessed using the ZBI. This scale contains 22 items and evaluates the impact of the patient's illness on the caregiver's life. Scores range from zero (no burden) to 88 (high burden) [32].
Depression	Depressive symptoms of caregivers were measured by the BDI-II, a brief scale consisting of 21 items. Scores range from zero to 63, with higher values indicating more significant depression [33].
Anxiety	The BAI consists of 21 self-reported items used for assessing the severity of anxiety. Scores range from zero to 63, with higher results indicating increased level of anxiety [34].

AD, Alzheimer's disease; ADAS-cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; ADL, activities of daily living; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; CDR, Clinical Dementia Rating scale; CSDD, Cornell Scale for Depression in Dementia; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; PFAQ, Pfeffer Functional Activities Questionnaire; ZBI, Zarit Burden Interview.

Statistical analysis

Descriptive statistics were used to illustrate the sample's characteristics. Differences between groups were tested with one-way ANOVA followed by post-hoc *t*-test adjusted with Bonferroni corrections, or chi-square test comparing gender and dementia severity.

Data analysis used the SPSS software (version 26.0), and alpha was set at 0.05.

RESULTS

We began by demarcating the groups by clinicians' ratings and ASPIDD scores. Clinicians classified PwAD with three alternatives, namely preserved awareness, impaired awareness, or absent awareness according to their answers related to cognitive functioning and health condition, functional impairments, emotional state, and social functioning and relationships. Meanwhile, ASPIDD scores demarcated four groups according to the discrepancy between AD patients' answers and caregivers' perceptions concerning questions that involved cognitive functioning and health condition, functional impairments, emotional state, and social functioning and relationships.

Differences in clinical aspects between groups of awareness according to clinicians' ratings

PwAD were first distributed in three groups according to the clinicians' ratings of their awareness (preserved awareness 25.4%, $n = 34$; impaired aware-

ness 67.1%, $n = 90$; absent awareness 7.4%, $n = 10$).

Table 1 shows the three groups' sociodemographic and clinical characteristics. No significant differences were found between groups in terms of age ($p = 0.379$), gender ($p = 0.442$), education ($p = 0.207$), or disease duration ($p = 0.217$). Depressive symptoms of PwAD (Cornell Scale for Depression in Dementia (CSDD), $p = 0.795$) and of caregivers (Beck Depression Inventory (BDI-II), $p = 0.402$) also failed to show significant differences between the three groups (Table 1).

Most PwAD in the preserved awareness group showed mild dementia (79.4%), while most individuals in the absent awareness group showed moderate dementia (80.0%) ($p = 0.001$). The preserved awareness group showed lower levels of cognitive deficits (MMSE, $p = 0.001$; Alzheimer Disease Assessment Scale – Cognitive Subscale (ADAS-cog), $p = 0.012$) and better functionality (Pfeffer Functional Activities Questionnaire (PFAQ), $p < 0.001$) when compared to the impaired and absent awareness groups. The absent awareness group showed more neuropsychiatric symptoms than the preserved and impaired awareness groups (Neuropsychiatric Inventory (NPI), $p = 0.017$).

In addition, according to impairment of awareness in the PwAD, caregivers showed significant differences between groups in terms of burden (Zarit Burden Interview (ZBI), $p = 0.005$) and anxiety (Beck Anxiety Inventory (BAI), $p = 0.008$), with more significant impairment in the absent awareness group (Table 1).

Comparison of the preserved and impaired awareness groups showed significant differences in cognition (MMSE, $p = 0.002$; ADAS-cog, $p = 0.01$), functionality (PFAQ, $p < 0.001$), neuropsychiatric symptoms (NPI, $p = 0.036$), and caregiver burden (ZBI, $p = 0.007$). No differences were found in caregivers' anxiety symptoms (BAI, $p = 0.051$).

Comparing the groups with preserved and absent awareness, differences were found in cognition (MMSE, $p = 0.027$), functionality (PFAQ, $p < 0.001$), neuropsychiatric symptoms (NPI, $p = 0.024$), and caregiver's anxiety symptoms (BAI, $p = 0.003$).

Comparison of the impaired and absent awareness groups only showed significant differences in caregivers' anxiety symptoms, with the absent awareness group showing more signs (BAI, $p = 0.038$).

Differences in clinical aspects between groups of awareness according to ASPIDD scores

PwAD were distributed in four groups according to ASPIDD awareness scores (preserved awareness 16.4%, $n = 22$; mildly impaired awareness 47.8%, $n = 64$; moderately impaired awareness 26.1%, $n = 35$; absent awareness 9.7%, $n = 13$).

Table 3 shows the four groups' sociodemographic and clinical characteristics. No significant differences were found between groups in terms of gender

Table 2
Description of sociodemographic and clinical characteristics according to clinician's rating of level of awareness

	Preserved ($n = 34$) Mean (SD)	Impaired ($n = 90$) Mean (SD)	Absent ($n = 10$) Mean (SD)	*p*
Age (y)	74.7 (9.2)	75 (9.4)	79.2 (6.9)	0.379
Gender (W/M) %	55.9/44.1	65.6/34.4	50.0/50.0	0.442
Schooling (y)	8.5 (4.2)	8.0 (4.0)	5.9 (3.8)	0.207
Disease duration (y)	4.3 (2.6)	5.4 (3.4)	4.6 (3.3)	0.217
CDR (1/2) %	79.4/20.6	48.9/51.1	20.0/80.0	0.001**
MMSE	20.4 (3.9)	17.5 (4.2)	16.5 (4)	0.001**
ADAS-cog	24 (9.9)	30.7 (11.7)	30.9 (9.5)	0.012*
PFAQ	11.8 (7.8)	19.5 (8)	24.2 (4.8)	< 0.001**
CSDD	7.4 (5.5)	8.1 (5.6)	7.4 (4.3)	0.795
NPI	11.7 (10.4)	20.1 (17)	25.2 (23.9)	0.017*
ZBI caregiver	23.3 (11.7)	32.7 (14.8)	36 (16.7)	0.005**
BAI caregiver	4.7 (3.8)	7 (6.2)	11.2 (8.6)	0.008**
BDI-II caregiver	7.3 (6.9)	7.6 (6.3)	10.5 (8.5)	0.402

CDR, Clinical Dementia Rating (CDR1: mild dementia; CDR2: moderate dementia); MMSE, Mini-Mental State Examination; ADAS-cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; PFAQ, Pfeffer Functional Activities Questionnaire; CSDD, Cornell Scale for Depression in Dementia; NPI, Neuropsychiatric Inventory; ZBI, Zarit Burden Interview; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory. $^{**}p < 0{,}01$ $^{*}p < 0.05$.

Table 3
Post-hoc test of significant clinical characteristics according to clinicians' ratings

	Preserved X Impaired			Preserved X Absent			Impaired X Absent		
	95% CI			95% CI			95% CI		
	Lower	Upper	*p*	Lower	Upper	*p*	Lower	Upper	*p*
MMSE	0.89	4.92	0.002**	0.34	7.54	0.027*	–2.30	4.37	1.000
ADAS-cog	–12.13	–1.24	0.01*	–16.60	2.86	0.267	–9.20	8.83	1.000
PFAQ	–11.48	–3.86	<0.001**	–19.16	–5.54	<0.001**	–10.99	1.63	0.224
NPI	–16.32	–0.40	0.036*	–25.01	–1.81	0.024*	–18.22	8.13	1.000
ZBI caregiver	–15.88	–1.93	0.007**	–24.59	0.35	0.06	–14.76	8.34	1.000
BAI caregiver	–5.23	0.54	0.153	–11.62	–1.31	0.009**	0.23	8.02	0.038*

CI, Confidence interval; MMSE, Mini-Mental State Examination; ADAS-cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; PFAQ, Pfeffer Functional Activities Questionnaire; NPI, Neuropsychiatric Inventory; ZBI, Zarit Burden Interview; BAI, Beck Anxiety Inventory; $^{**}p < 0.01$ $^{*}p < 0.05$ (adjusted by Bonferroni Correction).

($p = 0.303$), education ($p = 0.407$), or disease duration ($p = 0.149$). Caregivers' depressive symptoms ($p = 0.056$) and anxiety symptoms ($p = 0.232$) also failed to show significant differences between the four groups (Table 3).

Most PwAD in the preserved awareness (72.7%) and mildly impaired awareness (64.0%) groups showed mild dementia, while the moderately impaired awareness (62.9%) and absent awareness (77.0%) groups showed moderate dementia. Significant differences appeared between the four groups in relation to severity of disease ($p = 0.002$).

Comparing the groups, the absent awareness group was older ($p = 0.030$) and showed more significant impairments in cognition (MMSE, $p = 0.021$; ADAS-cog, $p = 0.043$), and functionality ($p < 0.001$) and presented more neuropsychiatric symptoms ($p = 0.014$). Regarding depressive symptoms, the moderately impaired awareness group showed more signs ($p = 0.031$), followed by the absent awareness group. Caregivers in the absent awareness group presented more burden (ZBI, $p = 0.036$).

In the group-by-group comparison, the preserved and mildly impaired awareness groups only differed in age ($p = 0.044$), where the preserved awareness group was younger. The preserved and moderately impaired awareness groups only differed in functionality ($p < 0.001$), where the preserved awareness group was more independent. Comparison of the preserved and absent awareness groups showed that the preserved group was younger ($p = 0.047$) and had better cognition ($p = 0.023$) and functionality ($p < 0.001$).

Compared to the mildly impaired group, the moderately impaired group showed more deficits in functionality ($p < 0.001$) and more depressive symptoms ($p = 0.037$). The mildly impaired and absent awareness groups only differed in functionality ($p < 0.001$), with the absent awareness group presenting more deficits.

No significant differences were found between the moderately impaired and absent awareness groups.

DISCUSSION

This study aimed to evaluate the clinicians' ratings and a discrepancy assessment method. We examined each group's demographic and clinical characteristics, comparing the groups according to their degree of awareness. The study's working hypothesis was that clinicians' ratings may not fully capture the heterogeneity of awareness, thus reducing its measurement accuracy. The ASPIDD scores reflect four degrees of awareness (preserved, mildly impaired, moderately impaired, and absent), while clinicians' ratings only present three degrees (preserved, impaired, and absent). We found that clinicians' ratings could not distinguish between the mildly and moderately impaired awareness groups, which has important implications for care, especially regarding autonomy and decision-making capacity, involving patients' decisions on treatment, institutionalization, and management of their property [16]. This aspect may limit the measurement's sensitivity.

Clinicians' ratings included individuals in the preserved awareness group who may have mildly impaired awareness. When PwAD are considered to have preserved awareness, it is assumed that they recognize deficits across all domains of the ASPIDD scale, and the responses match with caregivers' reports [23]. Our findings suggest that clinicians' ratings may not provide a reliable and comprehensive classification, unlike a multidimensional approach that can more effectively explore various aspects of awareness [35].

Table 4
Description of sociodemographic and clinical characteristics according to ASPIDD score

	Preserved ($n = 22$) Mean (SD)	Mildly impaired ($n = 64$) Mean (SD)	Moderately impaired ($n = 35$) Mean (SD)	Absent ($n = 13$) Mean (SD)	p
Age (y)	70.2 (9.8)	76.1 (8.4)	75.7 (9.3)	78.5 (9.4)	0.030*
Gender (W/M) %	54.6/45.4	70.3/29.7	54.2/45.8	53.8/46.2	0.303
Schooling (y)	8.0 (3.9)	8.3 (4.1)	8.0 (4.0)	6.2 (3.9)	0.407
Disease duration (y)	4.2 (2.9)	4.7 (3.0)	5.8 (3.7)	6.2 (3.6)	0.149
CDR (1/2) %	72.7/27.3	64.0/36.0	37.1/62.9	23.0/77.0	0.002*
MMSE	19.8 (3.9)	18.5 (4.4)	17.4 (3.7)	15.6 (4.2)	0.021*
ADAS-cog	26.0 (10.5)	27.3 (11.6)	32.2 (11.0)	34.0 (10.7)	0.043*
PFAQ	12.8 (8.5)	15.3 (8.0)	22.6 (6.3)	26.3 (3.4)	<0.001**
CSDD	8.8 (6.1)	6.4 (5.1)	9.5 (5.5)	9.0 (4.5)	0.031*
NPI	12.7 (8.3)	15.8 (18.2)	24.0 (12.3)	25.4 (23.2)	0.014*
ZBI caregiver	26.7 (11.7)	28.8 (14.1)	35.6 (15.3)	36.5 (17.8)	0.036*
BAI caregiver	4.3 (4.2)	7.3 (7.0)	7.3 (5.6)	7.1 (4.0)	0.232
BDI-II caregiver	8.1 (8.1)	6.5 (5.2)	10.2 (8.1)	6.6 (4.8)	0.056

CDR, Clinical Dementia Rating (CDR1: mild dementia; CDR2: moderate dementia); MMSE, Mini-Mental State Examination; ADAS-cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; PFAQ, Pfeffer Functional Activities Questionnaire; CSDD, Cornell Scale for Depression in Dementia; NPI, Neuropsychiatric Inventory; ZBI, Zarit Burden Interview; BAI: Beck Anxiety Inventory; BDI-II, Beck Depression Inventory. $^{**}p < 0.01$ $^{*}p < 0.05$.

Clinicians' ratings are still widely used in clinical practice and research. However, certain studies only use one or two questions to assess awareness [19], which can result in a superficial and subjective evaluation. We observed that clinicians based their evaluation of PwAD on different deficits, but the score was generic and did not specify the awareness domains. Clinicians' ratings are typically specific to a particular domain based on the questions used. Moreover, clinicians' perception of awareness in PwAD may be subject to bias, influenced by their experience, previous knowledge, and monitoring of the individual [19]. A questionnaire-based assessment thus seems more precise and responsive for measuring the awareness phenomenon and features more consistent administration for replication purposes [21].

When understanding how different groups of people relate to certain awareness measures, we expected that clinicians' ratings would be more closely linked to cognition and disease severity, while the ASPIDD score would be more associated with functionality than cognition. Our findings indicate differences between measures of awareness and that clinicians' ratings are affected more by various clinical factors beyond cognition and functionality. Meanwhile, the ASPIDD score appears to be driven primarily by functionality in group-to-group correlations. We plan to examine these differences in greater depth in future studies.

Differences in clinical aspects between groups of awareness according to clinicians' ratings

We categorized individuals with AD in three groups based on their awareness level as determined by clinicians: preserved, impaired, and absent. We hypothesized that clinicians' ratings of awareness would correlate more with cognition and disease severity. Our findings support existing research that suggests a link between impairment in awareness and cognitive decline in dementia, with deficits in awareness increasing as the disease progresses [12, 36]. Specifically, our results indicate that the preserved awareness group generally had mild dementia, while the absent awareness group tended to display moderate dementia.

As expected, disease severity and its cognitive and clinical symptoms were greater in the impaired awareness group compared to the preserved awareness group. Surprisingly, there were no significant differences between the impaired and absent awareness groups in terms of clinical symptoms in the PwAD. However, the absent awareness group showed the worst cognitive, functional, and neuropsychiatric symptoms and greater disease severity, regardless of disease duration. These results raise doubts about the influence of cognitive deficits on the awareness phenomenon, which is a complex construct that cannot be explained merely as a disease symptom. Although

Table 5
Post-hoc test of significant clinical characteristics according to ASPIDD score

	Pres X Mild imp			Pres X Mod imp			Pres X Abst			Mild imp X Mod imp			Mild imp X Abst			Mod imp X Abst		
	95% CI			95% CI			95% CI			95% CI			95% CI			95% CI		
	Lower	Upper	*p*	Lower	Upper	*p*	Lower	Upper	*p*	Lower	Upper	*p*	Lower	Upper	*p*	Lower	Upper	*p*
Age	0.11	11.74	0.044*	–0.91	11.88	0.120	.084	16.53	0.047*	–4.50	5.38	0.996	–4.77	9.53	0.822	–4.81	10.46	0.771
MMSE	–4.00	1.40	0.594	–5.41	0.53	0.149	–8.07	–0.42	0.023*	–1.16	3.43	0.575	–6.27	0.37	0.102	–5.36	1.73	0.546
ADAS–cog	–5.95	8.48	0.968	–1.79	14.10	0.188	–2.26	18.17	0.184	–11.02	1.25	0.168	–2.19	15.57	0.209	–7.68	11.28	0.960
PFAQ	–2.28	7.24	0.531	4.57	15.07	<0.001**	6.77	20.27	<0.001**	–11.39	–3.28	<0.001**	5.17	16.91	<0.001**	–2.56	9.96	0.419
NPI	–7.29	13.55	0.863	–0.17	22.77	0.055	–2.02	27.49	0.116	–17.03	0.69	0.083	–3.23	22.43	0.214	–12.26	15.13	0.993
CSDD	–5.89	1.03	0.268	–3.16	4.46	0.971	–4.69	4.11	0.999	–6.02	–0.12	0.037*	–1.62	6.90	0.376	–4.99	4.11	0.994
ZBI caregiver	–7.19	11.45	0.933	–1.36	19.16	0.114	–3.38	23.00	0.219	–14.70	1.16	0.123	–3.79	19.15	0.307	–11.34	13.16	0.997
BAI caregiver	–0.92	6.88	0.199	–1.35	7.25	0.285	–2.74	8.32	0.556	–3.29	3.35	1.000	–4.99	4.61	1.000	–5.29	4.97	1.000

Pres, Preserved awareness; Mild imp, Mildly impaired awareness; Mod imp, Moderately impaired awareness; Abst, Absent awareness; CI, Confidence interval; MMSE, Mini-Mental State Examination; ADAS-cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; PFAQ, Pfeffer Functional Activities Questionnaire; NPI, Neuropsychiatric Inventory; CSDD, Cornell Scale for Depression in Dementia; ZBI, Zarit Burden Interview; BAI, Beck Anxiety Inventory; $^{**}p < 0.01$, $^{*}p < 0.05$ (*p*-value and confidence intervals adjusted for comparing a set of 4 estimates).

deficits in awareness are related to disease severity when they are stable, as we have seen in the impaired and absent awareness groups, awareness can display different levels in these individuals, and cognition is no longer a significant aspect. This result may explain the discrepancies in awareness studies and why some longitudinal research has found that awareness is not a linear phenomenon [2, 9, 37]. Meanwhile, it is essential to note that awareness is a complex concept with multiple dimensions. To better understand any discrepancies in research findings, future studies must assess awareness across various domains and specify which ones were evaluated. The impaired and absent awareness groups only presented significant differences in terms of the anxiety symptoms experienced by their caregivers, which were more intense in the absent awareness group. Deficits in awareness cause some incapacities in PwAD that can contribute to caregiver distress, such as problems with treatment compliance and adherence, exposure to unsafe behavior, and increasing caregiver burden [38, 39]. In line with our results, a cluster analysis between groups (lower, moderate, and higher awareness) by Clare et al. [35] reported differences in cognition and caregiver distress, showing more intense anxiety symptoms in caregivers of patients with absent awareness. However, caregiver burden did not differ significantly between the group with absent awareness compared to the preserved and impaired awareness groups. Caregivers may experience a more significant burden in the early stages of the disease and become more adapted to the symptoms and behavioral changes. Bearing cultural differences in mind, caregivers in Brazil tend to receive peer support and are more attentive in interventions for PwAD, which may decrease their levels of burden [40]. The degree of awareness has essential implications for the caregiver's health and management and care for PwAD.

Moreover, awareness is proven to be affected by factors like functionality, neuropsychiatric symptoms, quality of life, cognition, and mood [18]. As the disease progresses, these features may affect the construct differently.

Neuropsychiatric symptoms are commonly experienced from the early stages of AD and tend to worsen with disease progression [41, 42]. Our study found that the preserved awareness group showed significant differences with the impaired and absent awareness groups, supporting previous research suggesting that the presence of neuropsychiatric symptoms, particularly irritability, and disinhibition

[43], are linked to deficits in awareness even in the early stages of the disease [42].

Differences in clinical aspects between the groups of awareness according to ASPIDD scores

Examining awareness according to initial ASPIDD scores, we grouped participants in four categories based on their level of awareness: preserved, mildly impaired, moderated impaired, and absent. Significant differences were found between groups in terms of age, disease severity, cognition, functionality, depressive and neuropsychiatric symptoms, and caregiver burden. Specifically, there were only significant differences between the preserved and absent awareness groups in the MMSE test. This suggests that awareness deficits vary among PwAD, even if they have similar levels of cognitive impairment. These findings are consistent with previous research suggesting that awareness is a complex and nonlinear phenomenon that is not necessarily linked to disease severity [9, 37, 44].

Meanwhile, both assessments showed a pattern of impairments in awareness and functionality. The level of impairment in activities of daily living (ADL) may relate intrinsically to preserved versus impaired awareness since the preserved awareness group may notice these deficits more quickly due to their more active daily routines. The relationship between awareness and functionality has been studied previously and shows that awareness is linked to the complexity of activities performed by PwAD [45–47]. The ASPIDD score did not show significant differences in functionality between the preserved and mildly impaired awareness groups or between the moderately impaired and absent awareness groups. Deficits in ADL follow a certain hierarchy in AD [48], whereby few difficulties are experienced at the onset of the disease, and only instrumental activities are affected and are not perceived as routine. However, with the progression of the disease and its deficits, PwAD may not notice the impairment in basic ADL, which is prominent in this stage of the disease.

Depressive symptoms exhibited an association between the mildly and moderated impaired awareness groups. We have observed that depressive symptoms fluctuate among the four groups. The mildly impaired group showed lower depressive symptoms compared to the other three groups. In contrast, the moderately impaired group displayed more significant depressive symptoms when compared to the other groups. Studies suggest that deficits in awareness are related to fewer depressive symptoms [11, 49], with depressive signs being an emotional reaction to the awareness of deficits [11]. Therefore, depressive symptoms may be related to the perception of cognitive deficits and greater dependence in ADL. However, another study failed to find this association [45].

As for caregiver symptoms, there were notable differences in the level of burden between the four awareness groups. However, no significant differences were found when comparing groups with each other. Burden is a multidimensional reaction to negative appraisal and perceived stress from caring for an ill individual [50]. Caregivers of individuals with dementia often experience high levels of stress and burden [51], and as previously mentioned, deficits in awareness can improve these symptoms independently of the level of awareness.

Some limitations should be analyzed when interpreting the study's results. First, the sample was recruited exclusively from an outpatient center for dementia, thus limiting generalization of the results to other PwAD. Future studies should thus include a control group from the community with less support and information about their condition to observe specificities in awareness. Moreover, although our study showed significant differences between groups, we did not assess each domain of awareness. Lastly, the clinicians' ratings were based on only three options (preserved awareness, impaired awareness, and absent awareness), whereas the ASPIDD score included four groups. This discrepancy could potentially impact comparisons between the two methods.

Our research has revealed that measuring awareness, a complex phenomenon, requires a highly sensitive approach to capture the various features and the different levels of awareness. Awareness can help in the assessment of clinical competence, and in a clinical setting, PwAD with preserved awareness can comprehend their disease and its consequences, thereby facilitating treatment compliance. Furthermore, understanding awareness and its predictors and differences across domains can help clinicians provide more personalized treatment.

Importantly, deficits in awareness differ according to the chosen method [52], and each measure has unique clinical implications. In clinicians' ratings, we observed that cognition and disease severity have more impact on evaluation. In the ASPIDD score, functionality plays the main role in differentiating the groups.

Our findings indicate that deficits in awareness may fluctuate throughout the disease progression. Patients in the moderate stage of AD can recognize their deficits, while those in the mild stage may not be aware of their impairment. Deficits in cognition and disease severity alone cannot fully explain deficits in awareness, which is a nonlinear phenomenon. Therefore, awareness assessment should be more sensitive to capturing nuances of the disease, especially since patients in the moderate stage may have some awareness of their illness.

AUTHOR CONTRIBUTIONS

Isabel Barbeito Lacerda, M.D. (Conceptualization; Investigation; Methodology; Writing – original draft; Writing – review & editing); Maria Alice Tourinho Baptista, PhD (Conceptualization; Investigation; Methodology; Writing – original draft; Writing – review & editing); Tatiana Belfort, PhD (Conceptualization; Investigation; Methodology; Writing – original draft; Writing – review & editing); Daniel Mograbi, PhD (Conceptualization; Methodology; Writing – original draft; Writing – review & editing); Marcia Cristina Nascimento Dourado, PhD (Conceptualization; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing).

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CONFLICT OF INTEREST

Marcia C.N. Dourado is an Editorial Board member of this journal but was not involved in the peer-review process of this article nor had access to any information regarding its peer review.

DATA AVAILABILITY

The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to ethical and privacy restrictions.

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