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ORIGINAL ARTICLE

Spanish adaptation and validation of the ALS Depression Inventory-12 (ADI-12) in patients with Amyotrophic Lateral Sclerosis

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Background. Patients with Amyotrophic Lateral Sclerosis (ALS) have a higher prevalence of mood disorders, including depression, than the general population. Non-specific measurement instruments have been used to evaluate depression in these patients, which complicates accurate diagnosis. The ALS Depression Inventory (ADI-12) exclusively assesses depressive symptoms in patients with ALS.

Aim. To adapt and validate the ADI-12 in a Spanish sample.

Methods. A selective design was used with 74 patients with ALS, using the ADI-12 questionnaire. The original instrument was translated and back-translated into Spanish. The internal structure, temporal stability, convergent, and discriminant validity of the instrument were analyzed.

Results. Two confirmatory models showed internal validity ($p = 0.502$ for the one-factor model, $p = 0.507$ for the two-factor model). The Cronbach's alpha (0.900 in the first measurement and 0.889 in the second one) indicated a high internal consistency of the test. The Pearson correlation (0.90) indicated high temporal stability. In terms of convergent validity, the ADI-12 showed moderate correlations with the Beck Anxiety Inventory (BAI) (0.51–0.58), and low correlations with time since ALS diagnosis (–0.26 to –0.27).

Limitations. The main limitation of the present study was the small sample size.

Conclusions. The ADI-12 is fitted to a single general factor of depression, and the scale shows high internal consistency and high temporal stability, therefore, its use is recommended for the diagnosis of depression in patients with ALS.

Key Words: ADI-12, Amyotrophic Lateral Sclerosis, Depression, Anxiety.

Introduction

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that affects motor neurons responsible for voluntary motor control and progressively impacts the quality of life of patients and their families (1–3). There is no cure, so therapeutic measures focus on controlling symptoms and improving quality of life (2,4). ALS has a high mortality rate and a low prevalence, ranging from two to five cases per 100,000 inhabitants (5–7). Its worldwide incidence is 1.75/100,000 inhabitants per year with higher rates in males (2,03/100,000 in males and 1,45/100,000 in females), with an incidence increase in recent years (7). In

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Spain, the prevalence and incidence of ALS are similar to those in other countries, with an annual crude incidence rate of 1.4/100,000 (5,8) and higher incidence in males at 1.6/100,000 compared to 1.2/100,000 in females (9).

Regarding diagnosis, the average age of onset is 60–69 years (a median of 65 years with no differences between sexes), with a peak incidence at 70–75 years that decreases in older ages (5,8,9). Life expectancy from the diagnosis of ALS is less than five years (usually due to progressive respiratory failure) (5,9).

Manifestations of ALS include motor and, to a lesser extent, non-motor symptoms, such as neuropsychiatric disturbances, as well as cognitive and behavioral disorders, including cognitive impairment and apathy (10,11), with an increasing prevalence of these types of alterations (12). These symptoms are predictors of medium- and long-term disability (13).

Depression in Patients with ALS

According to the International Classification of Diseases in its 11th edition (ICD-11), depressive disorders are characterized by a depressive mood (e.g., sadness, irritability, feeling of emptiness) or loss of pleasure, accompanied by other cognitive, behavioral, or neurovegetative symptoms that significantly affect the individual's functional capacity (14). According to the DSM 5-TR taxonomy (15), diagnostic criteria for depressive disorder include a depressed mood for most of the day, a significant decrease in interest or pleasure in activities, fatigue or loss of energy, or decreased ability to think, concentrate, or make decisions.

In patients with ALS, depression tends to co-occur with anxiety disorders, among others, and diagnosis is often confused with apathy (16). A recent study conducted in Scotland found a prevalence of 19.7% of neuropsychiatric disorders in patients with ALS, of which 70% were mood disorders (17). The prevalence of these disorders in people with ALS is higher than that of the general population, with 6.9% of patients suffering from depressive disorders and 14% diagnosed with some form of anxiety disorder (18). Prado R, et al. (12), found a depression prevalence of 10–40% in a sample of patients with ALS in Brazil, although there is wide variability in findings depending on the type of study and instruments used (4,13).

Measuring Depression in ALS. The ADI-12 Scale

Traditionally, depression in patients with ALS has been measured using instruments that were not specific to the disease (19) and included other variables related to motor abilities, which hamper accurate diagnosis (16). These instruments include the Hospital Anxiety and Depression Scale (HADS) (20), and the Neuropsychiatric Inventory (NPI) (21), which measure delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, aberrant motor activity in patients with dementia, the Beck Depression Inventory (BDI) (22); the Hamilton Depression Rating Scale (HDRS) (23), and the Patient Health Questionnaire (PHQ-9) (24).

To eliminate bias in the evaluation of depression in patients with ALS, Kübler A, et al. (25) developed the ALS Depression Inventory (ADI-12) to assess depressive symptoms only. The German scale consists of 12 four-point Likert-type items and was validated in a sample of 76 German patients with ALS. Using varimax rotation in principal component analysis, they identified a general component that explains 94.6% of the variance in the items. The test showed high internal consistency (Cronbach's α of 0.87–0.95). There were no differences based on sex, and the correlation between the scale and age was very low ($r = 0.08$). The scale assesses a homogeneous and unidimensional construct described as "mood, anhedonia, and energy".

Hammer E, et al. (26) used the ADI-12 on another German sample of 37 patients with ALS and obtained high internal consistency (Cronbach's α of 0.8–0.9). Convergent validity evidence with depression (according to the BDI) was analyzed, and a high correlation ($r = 0.81$) and a psychological well-being scale ($r = –0.64$) were obtained. Moreover, the diagnostic classification value of the ADI-12 for major depression was high, with a sensitivity of 100% and a specificity of 83% for a cut-off point $\geq$30 on the scale.

The ADI-12 scale has been translated into Portuguese (19), although not validated, and adapted and validated in Italian (16). The Italian validation was carried out in 85 patients with ALS, and the internal structure of the scale was analyzed using a principal component analysis with oblique rotation. Two related components were found ($r = 0.48$) that explained 61.02% of the variance of the scale. The first component was identified as negative mood and lack of energy (seven items), and the second was anhedonia (five items). The first component's internal consistency (Cronbach's α) was 0.86, the second was 0.84, and the total scale was 0.90. Evidence of convergent validity was examined by relating the scale to measures of anxiety ($r = 0.18$ to 0.42), depression ($r = 0.42$–0.54), and quality of life ($r = –0.34$ to –0.59). Finally, the classification of the ADI-12 for depression was analyzed, obtaining a sensitivity of 88.9% and a specificity of 69.4% for a cut-off point of 27.5.

The questionnaire to measure depression in ALS only had a German and an Italian version with valid data. Therefore, it was necessary to translate and adapt it to a Spanish sample, especially considering that the prevalence of this disorder is higher in these patients than in the general population (18). The two versions of the ADI-12 validated their internal structure by principal component analysis, whereas the recommended procedure is to use maximum likelihood and oblique rotation to extract the factors

(27). The principal components extract common and specific variance from different indicators (items), inflating the percentage of explained variance. Moreover, it is recommended to extract only common variance when extracting common factors. There is also a discrepancy in the dimensionality of the test, with one case finding only one factor (27) and another finding two correlated factors (16).

Aims

The general objective of this study was to adapt and validate the ADI-12 in a cohort of Spanish patients with ALS. Thus, we aimed to a) calculate the internal validity evidence of the ADI-12 using confirmatory factor analysis, to determine whether the data fit better with one or two related dimensions; b) estimate the reliability of the test by analyzing internal consistency and temporal stability; c) obtain evidence of convergent and discriminant validity by relating the test to anxiety, age, and time since ALS diagnosis; d) calculate the evidence of differential validity by comparing ADI-12 results based on sex and type of ALS (bulbar and spinal); and 5) establish norms for the test to be clinically useful.

Material and Methods

Participants

The sample consisted of patients with clear symptoms of ALS, diagnosed according to the El Escorial diagnostic criteria (28), with at least six months of disease duration, and over 18 years of age. Patients with a tracheostomy, invasive or non-invasive positive pressure ventilation, evidence of dementia, or evidence of alcohol or drug abuse were excluded. The sample included 74 patients with a mean age of 55.9 years (SD = 10.4 years, range 28–76 years), of whom 65.3% were male. Ten patients had bulbar ALS, 62 had spinal ALS, and two were undetermined. The mean time since diagnosis was 28.62 months (SD = 28.27 months) with a range of 2 to 146 months. The sample size ($n = 74$) may seem small for the validation of a scale, but ALS has a low incidence worldwide (1.75/100,000 inhabitants/year) (7). Previous studies have had similar sample sizes: $n = 75$ (25), $n = 37$ (26) and $n = 85$ (16). The sample also included a higher number of males, which is consistent with a higher incidence in males (1.6/100,000) than females (1.2/100,000) (9).

Instruments Used

ALS Depression Inventory-12 (25). The instrument comprises 12 items to measure depressive symptoms in patients with ALS while excluding the increasing physical damage inherent to the disease. The assessment considers the mood of the last two weeks, and the response format is a four-point Likert scale ("Strongly agree" to "Strongly disagree"). See the Spanish Version in the supplemental material.

The Beck Anxiety Inventory (BAI) (29) in its Spanish version by Sanz and Navarro (30) was used. This is a 21-item self-report inventory designed to assess the severity of anxiety symptoms. Each item assesses an anxiety symptom, and respondents rate the degree to which they have been affected by it during the past week using a four-point Likert scale ("Not at all" to "Severely, I could hardly stand it"). The BAI measures two highly correlated anxiety dimensions: somatic and affective-cognitive. Table 1 shows the internal consistency values for the test and its two dimensions.

Design and Procedure

A selective design was used with participants who had been diagnosed with ALS for at least six months and were over 18 years of age.

First, the ADI-12 was translated according to the guidelines of Guillemin F, et al. (31):

- Translation from English to Spanish. This involved two independent translations by two bilingual translators (English-Spanish) whose native language was Spanish. A consensus version of the instrument, originally published in English by Hammer E, et al. (26), was reached after both translators discussed the two versions and resolved discrepancies.
- Reverse translation. The agreed-upon version of the ADI-12 was back-translated into English by a professional translator whose native language was English and who was not familiar with the topic under study.
- Revision. The reverse translation version was compared with the original, and adjustments were made to ensure that both versions conveyed the same meaning.

The project was approved by the Clinical Research Ethics Committee of Hospital La Fe in Valencia, Spain (2021-001989-38). To recruit participants, associations of patients with ALS in Spain were contacted by e-mail and phone. It was explained that participation in the study was voluntary, anonymous, and without financial compensation. Participants received information about the study before completing the questionnaires. The ADI-12 and BAI were applied twice, at a two month interval, under the supervision of members of the research group.

Data Analysis

The statistical software AMOS V. 23 (32) was used to analyze internal structure of AD-12. Goodness-of-fit was assessed using several indices for confirmatory factor analysis (33–37). All other analyses were conducted with the

Table 1. Descriptive statistics for the ADI-12 and BAI items, internal consistency, corrected item-total correlation ($r_{item\text{-}test}$) and initial communality (h^2)

	Mean	SD	Asymmetry	Kurtosis	Cronbach's α	$r_{item\text{-}test}$	h^2
ADI-12 item 1	0.84	0.76	0.67	0.22		0.71	0.60
ADI-12 item 2	0.77	0.82	0.91	0.36		0.59	0.47
ADI-12 item 3	1.05	0.87	0.91	0.48		0.55	0.40
ADI-12 item 4	0.92	0.96	0.74	-0.48		0.66	0.53
ADI-12 item 5	1.26	0.92	0.00	-1.03		0.63	0.46
ADI-12 item 6	0.26	0.50	1.80	2.49		0.54	0.41
ADI-12 item 7	0.62	0.89	1.19	0.31		0.72	0.61
ADI-12 item 8	0.55	0.85	1.43	1.15		0.68	0.63
ADI-12 item 9	0.57	0.85	1.39	1.07		0.72	0.58
ADI-12 item 10	1.04	1.03	0.62	-0.76		0.48	0,30
ADI-12 item 11	0.49	0.83	1.66	1.85		0.71	0.57
ADI-12 item 12	1.19	0.95	0.11	-1.10		0.54	0.43
ADI-12 Total Pre-test	9.55	7.13	1.33	2.20	0.900		
ADI-12 Total Post-test	8.96	7.07	1.36	1.52	0.899		
BAI Somatic Anxiety Pre-test	20.99	7.21	1.02	0.70	0.891		
BAI Affective-Cognitive Anxiety Pre-test	18.42	7.21	1.08	0.51	0.912		
BAI Total Anxiety Pre-test	35.73	12.58	1.11	0.71	0.939		
BAI Somatic Anxiety Post-test	20.46	6.99	1.04	0.50	0.879		
BAI Affective-Cognitive Anxiety Post-test	17.70	6.45	1.13	1.37	0.886		
BAI Total Anxiety Post-test	34.69	11.70	1.11	0.95	0.927		

statistical software SPSS V. 18. Data is expressed as mean and standard deviation or median and interquartile ranges according with variablesdistribution. Percentile, Z-scores, normalized Z-scores, and T-scores were calculated for ADI-12 raw data.

For factorial analysis, the ratios for the two models tested were 12/1 = 12 for one-factor model and 12/2 = 6 for two-factor model, with initial commonalities between 0.30 and 0.63 (Table 1) and n = 74, as suggested by some authors (36,38,39).

Reliability was estimated using Cronbach's α for internal consistency and Pearson correlation between the two measures obtained from ADI-12 test-retest reliability. Correlations between each item and the total corrected score were estimated to examine internal discrimination. Convergent and discriminant validity was obtained from Pearson correlation coefficients between ADI-12 and measures of anxiety, age, and months from diagnosis. Differential validity for sex and the type of ALS was evaluated with student *t*-test.

Results

Descriptive Analysis

Table 1 shows the descriptive statistics for the 12 items of the ADI-12, the total test score, the two dimensions, and the total BAI for both applications. For all measures, the asymmetry is not greater than two, and the kurtosis is not greater than seven in absolute value, so the 12 test items are suitable for using the maximum likelihood procedure (40).

Evidence of Internal Validity

Following two previous studies on ADI-12, two confirmatory models were estimated, one with two factors and another with one general factor (Figure 1). Both models showed multivariate normality using Bollen-Stine bootstrapping (41) ($p = 0.502$ for the one-factor model, $p = 0.507$ for the two factor model). The goodness-of-fit indices of both models are similar and indicate a good fit of the models to the data (Table 2). The factor weights of the items exceeded the recommended minimum of 0.40 (36), indicating that all items contribute significantly to the formation of the latent factors. In the case of the two factor model, a factor of "Lack of energy and negative mood" was formed by seven items, and another factor of "Anhedonia" was made up of five items. The correlation between these two factors is very high ($r = 0.97$), which would indicate that they are the same duplicated factor. Therefore, following the principle of parsimony, it seems more sensible to consider the 12 items grouped in a general depression factor.

Evidence of Scale Reliability

The internal consistency of the ADI-12 scale, as measured by Cronbach's α, presents a very high value: 0.900 in the first measurement and 0.889 in the second one. Furthermore, the corrected item-total correlation is above 0.40 in all cases, indicating a high internal discrimination of the test (Table 1) (36). The test-retest reliability, calculated with the Pearson correlation between these two measurements, is 0.90, indicating high stability.

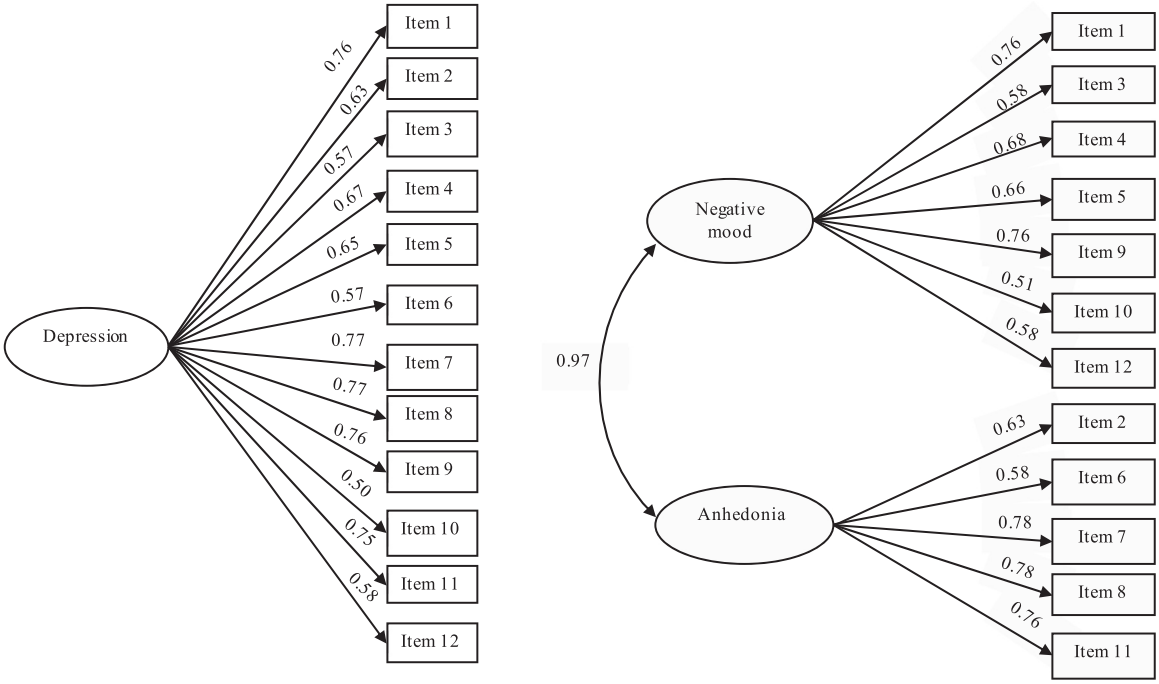

Figure 1. 1-factor model (left) and 2-factor model (right) for the items of the ADI-12.

Table 2. Goodness-of-fit indices for the 1- and 2-factor models of the ADI-12

Model	χ^2/df	GFI	NFI	CFI	TLI	PGFI	PNFI	PCFI	RMSEA	SRMR
1 factor	1.190	0.874	0.854	0.973	0.966	0.594	0.686	0.781	0.051	0.062
2 factors	1.198	0.874	0.856	0.972	0.964	0.583	0.675	0.766	0.052	0.061

Table 3. Pearson correlations among ADI-12, BAI, age, and time since ALS diagnosis

	1	2	3	4	5	6	7	8	9	10
1. Age	1.00									
2. Diagnosis time (months)	-0.02	1.00								
3. ADI-12 Pre-test	0.11	-0.26	1.00							
4. ADI-12 Post-test	0.08	-0.27	1.00	1.00						
5. BAI Somatic Anxiety Pre-test	0.04	-0.07	0.50	0.49	1.00					
6. BAI Affective-Cognitive Anxiety Pre-test	0.00	-0.17	0.47	0.45	0.83	1.00				
7. BAI Total Anxiety Pre-test	0.01	-0.12	0.52	0.50	0.95	0.96	1.00			
8. BAI Somatic Anxiety Post-test	-0.06	-0.11	0.52	0.40	0.83	0.67	0.78	1.00		
9. BAI Affective-Cognitive Anxiety Post-test	-0.05	-0.14	0.58	0.46	0.76	0.82	0.83	0.84	1.00	
10. BAI Total Anxiety Post-test	-0.06	-0.12	0.58	0.46	0.83	0.77	0.84	0.96	0.96	1.00

The correlations $\geq |\pm 0.26|$ are statistically significant at the 5% level.

Evidence of Convergent and Discriminant Validity

Pearson correlations were calculated between the ADI-12, in the two temporal measurements, with the dimensions of the BAI, the age of the subjects evaluated, and the time since diagnosis of ALS. Table 3 shows the results obtained. Regarding convergent validity, the ADI-12 shows moderate correlations with the BAI (0.51–0.58), and low correlations with the time of ALS diagnosis (–0.26 to –0.27). This indicates that patients with ALS with depression also tend to have anxiety and that depression tends to decrease as time goes by. Regarding discriminant validity, the ADI-12 is not related to patient age (0.08–0.11).

Evidence of Differential Validity

An analysis was conducted using independent *t*-tests to determine if there were differences in depression scores on the ADI-12 based on patients' sex and type of ALS. No statistically significant differences were found for either sex (t70 = 0.57, $p = 0.569$) or type of ALS (t70 = 0.69,

Table 4. Descriptive statistics for sex and type of ALS in the ADI-12

	n	Mean	SD
Male	47	9.34	6.97
Female	25	10.36	7.63
Bulbar ALS	10	12.00	11.96
Spinal ALS	62	9.32	6.14

Table 5. Norms for the ADI-12

	Direct score	Centile	Z	Z_n	T
	0.00	1	-1.34	-2.33	26.70
	0.75	5	-1.23	-1.64	33.60
	2.00	10	-1.06	-1.28	37.20
	3.00	15	-0.92	-1.04	39.60
	3.00	20	-0.92	-0.84	41.60
	4.75	25	-0.67	-0.67	43.30
	5.00	30	-0.64	-0.52	44.80
	6.00	35	-0.50	-0.39	46.10
	7.00	40	-0.36	-0.25	47.50
	7.00	45	-0.36	-0.13	48.70
	7.50	50	-0.29	0.00	50.00
	10.00	55	0.06	0.13	51.30
	10.00	60	0.06	0.25	52.50
	11.00	65	0.20	0.39	53.90
	12.00	70	0.34	0.52	55.20
	13.00	75	0.48	0.67	56.70
	14.00	80	0.62	0.84	58.40
	16.00	85	0.90	1.04	60.40
	18.00	90	1.19	1.28	62.80
	26.00	95	2.31	1.64	66.40
	26.00	99	2.31	2.33	73.30
Mean	9.55		0.00	0.00	50.00
SD	7.13		1.00	1.00	10.00

$p = 0.504$). Thus, it is not appropriate to assume that there are differences between these two variables in the means of depression scores (Table 4).

Table 5 presents the normative criteria for individuals evaluated with the ADI-12. Specifically, for each raw score, the corresponding percentile score, standardized score (Z-score), normalized Z-score, and T-score were calculated (M = 50, SD = 10). These data will allow future evaluators to determine whether an individual with ALS has a high level of depression in comparison to the sample in this study. Norms were not calculated separately for sex and type of ALS because there were no differences in the questionnaire responses for these variables.

Discussion

A depression measurement tool (ADI-12) was adapted and validated for use with patients with ALS. The tool had previously been validated in a German (25) and an Italian (16) sample with similar characteristics. Although ALS is a disease with low prevalence (two to five cases per 100,000 inhabitants) (5–7) and low incidence (1.75/100000) (7), depression is more prevalent in patients with ALS (6.9%) compared to the general population and is associated with anxiety in 14% of cases (18). Therefore, it is reasonable to have a depression assessment tool tailored to patients with ALS.

The results of our study indicate that the factor structure of the ADI-12 fits a single general depression factor, as previously found by Kübler A, et al. (25) in a German sample, and do not support the two factor result obtained in an Italian sample (16), since in our case the two factors proposed in that study show an almost perfect correlation ($r = 0.97$), suggesting a better fit for a single general factor. Furthermore, in this study, the factor solution was obtained through a confirmatory procedure and maximum likelihood estimation, while other authors incorrectly used a principal component analysis (16,25).

Regarding the evidence of reliability, very high values of internal consistency were obtained ($\alpha = 0.889$–0.900), similar to previous studies (16,25,26). A high temporal stability of the scale between the two measures was also observed in the same participants ($r = 0.90$), a finding not previously reported.

The analysis of the evidence of convergent and discriminant validity also shows results consistent with previous studies. For convergent validity, moderate correlations were observed between the scale and anxiety ($r = 0.51$–0.58), as previously found by Pain D, et al. (16), and for discriminant validity, no relationship with age was found, consistent with previous studies (25). In addition, another measure of convergence was also obtained between the ADI-12 and time since diagnosis ($r = -0.26$ to -0.27), suggesting that patients tend to have fewer depressive symptoms as time passes. Similarly, no sex differences in the ADI-12 were found, as previously reported (25), nor on the type of ALS (bulbar or spinal) either. The latest novelty of the study is the calculation of norms for those evaluated on the scale, which will be useful for future evaluations of depression in ALS.

It would be interesting to conduct future research for further evidence on the ADI-12, such as its usefulness as a diagnosis compared to other clinical procedures, as documented in the literature (16,26). Moreover, it would be valuable to correlate the scale to other measures of quality of life and psychological well-being to provide further evidence of convergent validity, as has been observed previously (16,26). The scale's sensitivity to change could also be analyzed by applying it before and after an intervention aimed at reducing depression, and a larger sample could be obtained to confirm the results.

Limitations

The main limitation of this study is the small number of participants ($n = 74$), which may hinder the validation of a test. Nonetheless, the indicator/factor ratio and the commonalities obtained in the study suggest that these results

have more than 87% agreement with the reference population based on previous simulations (39).

Conclusions

In summary, the Spanish validation of the ADI-12 in a sample of patients with ALS provides significant advantages for research and clinical purposes, supporting the use of this questionnaire in this type of patients due to its excellent psychometric properties.

Conflicts of Interest

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.arcmed.2023.102936.

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