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Quality of life in patients with mild cognitive impairment

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Quality of life in patients with mild cognitive impairment

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Background: Quality of life (QoL) is affected in patients with dementia, but it is not clear whether it is already disturbed in more initial phases of cognitive decline, like Mild Cognitive Impairment (MCI).
Aim: Compare the QoL in MCI patients with controls without cognitive impairment, and ascertain whether there are differences in the reports of QoL made by the subjects and by their informants.
Methods: Two hundred participants were enrolled, divided into MCI patients ($n = 50$), MCI informants ($n = 50$), recruited from a memory clinic and a dementia outpatient clinic, and controls ($n = 50$) and controls informants ($n = 50$), recruited in a family practice clinic. QoL was assessed with the QoL in Alzheimer disease (QOL-AD) scale.
Results: The total scores of the QOL-AD questionnaire were 32.1 ± 6.9 for MCI patients self-report, 27.2 ± 6.7 for MCI patients in the opinion of their informants, 35.3 ± 4.9 for controls self-report and 35.6 ± 4.9 for controls in the opinion of their informants. MCI patients had lower QOL-AD scores than controls. The QoL reported by patients with MCI was more favorable than the opinion of their informants.
Conclusion: The QoL is affected at early stages of cognitive decline. The QoL reported by patients with MCI is better than the opinion of their informants, similarly to what is known in Alzheimer's disease patients. QoL appears to be an important domain to be evaluated in aging studies.

Keywords: QOL-AD; MCI; Alzheimer's disease; caregiver-report; self-report

Introduction

Quality of Life (QoL) is recognized as an increasingly important healthcare topic to ascertain the real impact of disease and treatment in human life, particularly in chronic disorders (Muldoon, Barger, Flory, & Manuck, 1998). The World Health Organization (1995) defined QoL as *the individual's perception of their position in life in the context of culture and value system in which they live, and in relationship to their goals, expectations, and standards*. This definition assumes that individuals have the intellectual capacity to make complex subjective judgments about their lives. Many questions have been raised about the ability of persons with dementia to make such judgments and about the point at which they become unable to do so. Assessing QoL in cognitively impaired older adults certainly poses unique challenges because QoL is a complex process that involves many cognitive abilities such as attention, memory, language, and abstract thinking which are likely affected in these patients (Logsdon, Gibbons, McCurry, & Teri, 2002). Nevertheless, QoL has been identified as an important domain for dementia assessment (Lawton, 1994). Furthermore, QoL is an indicator of the overall impact of interventions for individuals with dementia, and improving QOL has been advanced as a primary

goal of dementia treatment (Logsdon, McCurry, & Teri, 2007).

QoL was indeed found to be affected in patients with dementia, more so in the opinion of the caregivers than of the patients themselves (Conde-Sala, Garre-Olmo, Turró-Garriga, López-Pousa, & Vilalta-Franch, 2009; Hurt et al., 2008; Ready, Ott, & Grace, 2004; Thorgrimsen et al., 2003; Vogel, Mortensen, Hasselbalch, Andersen, & Waldemar, 2006). However, more pronounced cognitive deficits or greater limitations in daily activities are not necessarily reflected in lower QoL in patients with dementia (Banerjee et al., 2009). It is controversial whether QoL is already disturbed in more initial phases of cognitive decline, like Mild Cognitive Impairment (MCI), a clinical entity now accepted in both clinical practice and research that entails a high risk of progression to dementia. Some researchers found that QoL is not affected in MCI patients (Missotten et al., 2008; Ready et al., 2004) while other detected that some aspects of QoL are altered (Muangpaisan, Assantachai, Intalapaporn, & Pisansalakij, 2008).

Several instruments have been validated to evaluate QoL in patients with cognitive decline and dementia. In the present study, we used the QOL-AD scale, a short, self-characterization instrument that can be

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completed by patients unless severely demented and is able to provide both the caregivers' and the patients' point of view (Logsdon et al., 2002). The objective of the present work was to ascertain whether patients with MCI have a decrease in the QoL as compared to subjects without cognitive impairment. Additionally, we aimed to compare the reports of QoL made by the subjects and by their informants, both in MCI patients and in subjects without cognitive impairment.

Materials and methods

Participants

Participants were patients with MCI, and their informants (MCI-informants), attending a memory clinic and a dementia outpatient clinic. Controls and their informants (controls-informants) were recruited in a family medicine outpatient clinic. The study was approved by the Ethics Committee of Hospital de Santa Maria. Before any procedure, participants gave written informed consent.

Inclusion criteria for MCI group were based on European Consortium on Alzheimer's Disease (Portet et al., 2006). For reasons of sample homogeneity, only patients with the amnestic type of MCI (aMCI) were recruited:

(1) Cognitive complains and cognitive decline during the last year, reported by the patient and/or family.
(2) Objective memory impairment, as defined by a low score in immediate free recall of *story A* from logical memory (LM) subtest of Wechsler Memory Scale (see below).
(3) Maintained activities of daily living or slight impairment in instrumental activities of daily living (IADL), as defined by no more than one item of IADL changed (see below).
(4) Absence of dementia, according to DSM-IV, and normal Mini Mental State Examination (MMSE) scores (see below).
(5) Age ≥50 years.

Inclusion criteria for MCI-informants, controls and controls-informants:

(1) Absence of cognitive complaints.
(2) Normal score in immediate free recall of *story A* from LM subtest of Wechsler Memory Scale (see below).
(3) Maintained activities of daily living as defined by IADL (no item of IADL changed, see below).
(4) Absence of dementia, according to DSM-IV, and normal MMSE scores (see below).
(5) Age ≥50 years for controls (age was not a criterion for informants).

Exclusion criteria for all groups:

(1) History of alcohol abuse or recurrent substance abuse or dependence.

(2) Other neurological, psychiatric or medical disorders that might induce cognitive deficits.
(3) Major depressive episode according to DSM IV, or severe depressive symptoms as reflected by a score in the 15 item Geriatric Depression Scale (GDS_{15}) > 10 (see below).
(4) Education (schooling years) less than four years.

Procedures

A separate interview with patients or controls and their informants was conducted. The informants were close relatives who knew the patient/control well. Demographic data (age, sex, education, marital status, and occupation) and clinical data were collected during the interview for all participants.

MCI patients underwent a standard protocol with clinical history, neurological examination, laboratorial evaluation, and brain imaging (CT scan or MRI scan) (Knopman et al., 2001), and a detailed neuropsychological evaluation with the Battery of Lisbon for Evaluation of Dementia (Garcia, 1984).

All participants were submitted to the Portuguese versions (de Mendonça & Guerreiro, 2008) of the following instruments:

(1) MMSE (Folstein, Folstein, & McHugh, 1975), MMSE is widely used for brief evaluation of the mental state and screening of dementia. The normative cut-off values for the Portuguese population adjusted to education were used (Guerreiro, Silva, & Botelho, 1994). Subjects should score above 22 if they had ≤11 years of education, or above 27 if they had >11 years of education.
(2) LM subtest from the Wechsler Memory Scale (Wechsler, 1969), which is included in the Battery of Lisbon for the Evaluation of Dementia (Garcia, 1984). Memory was considered impaired when the subjects scored on immediate free recall of story A of the test at least 1.5 standard deviation (SD) below the normative value for age and education.
(3) IADL (Lawton & Brody, 1969). The IADL score reflects the number of impaired activities and ranges from 0 (no impairment) to 8 (changes in all items). Items were classified as not applicable if the activity had never been done before or if the subject stopped doing it for reasons other than cognitive difficulty. Activities of daily living were considered preserved if no item from the IADL scale suffered any change, or mildly affected if only one item from the IADL scale was altered (Pantoni et al., 2005).
(4) GDS (Yesavage et al., 1983). The GDS is a self-report depression assessment scale used specifically to evaluate depression in the elderly. The 15 item version was used for this study.

(5) Satisfaction with Life Scale (SWLS; Diener, Emmons, Larsen, & Griffin, 1985). This scale assesses global life satisfaction reflecting subjective well-being.

(6) QOL-AD scale (Logsdon et al., 2002). The QOL-AD scale is a short, self-characterization instrument that can be completed by patients unless severely demented. It comprises 13 items within five domains: 'perceived QoL', 'behavioral competence', 'psychological status', 'interpersonal environment' and 'physical functioning'. QOL-AD uses simple and straightforward language. Responses are structured in a four-choice format for all the items and the total score is obtained by adding the score of individual items. The total scores range from 13 to 52 and lower points are associated with worse QoL. One of the main advantages of QOL-AD is that it can provide both caregiver and patient point of view. Each individual completed the scale alone, as instructions were read. For those participants with reading difficulties the interviewer would circle the answer.

(7) Charlson, Pompei, Ales, and McKenzie (1987) Index. This index measures the presence of 22 pre-set conditions, with a relative weight for each pathology. Increasing scores indicate higher mortality risk. In the original study, one year mortality rates for the different scores were: '0', 8%; '1–2', 26%; '3–4', 52%; '≥5', 85%.

Of the 214 participants initially evaluated, 14 were excluded from the study for the following reasons: severe depression at the time of the evaluation ($n = 12$) and lack of collaboration from the accompanying relative ($n = 2$).

Statistical analysis

Statistical Analysis was performed using Statistical Package for the Social Sciences (SPSS 19.0. SPSS INC: IBM). The significance level used for all analysis was $p < 0.05$.

Comparison of demographic characteristics among the four groups was made with one-way ANOVA for numerical variables and the chi-square test for categorical variables. Comparison of Charlson index

between MCI and control subjects was made with the Student's *t* test for independent variables.

Differences in MMSE, LM, GDS, and SWLS among the four groups were analyzed with one-way ANOVA, followed by *post-hoc* Tukey's test when appropriate. Since for both MCI patients and controls, two QOL-AD reports were available (the own report and the informant's report), analysis of QOL-AD total score was done with repeated measures ANOVA. The within-subjects analysis compared the subjects' own report with the report of their informants. The between-subjects analysis compared MCI patients with controls.

Comparison of scores of individual QOL-AD items was done with one-way ANOVA. Analysis of differences between MCI and control self-reports, and between MCI self report and informant report, was performed with the *post-hoc* Dunnett test (MCI self-report was the reference group). Since, this was an exploratory analysis, no correction for multiple comparisons was done.

Results

The study recruited 200 participants, divided into four groups: MCI patients ($n = 50$), their informants (MCI-informants, $n = 50$), controls ($n = 50$) and their informants (controls-informants, $n = 50$). There were no statistical differences among the groups regarding demographic variables (Table 1). MCI informants were spouses (38), sons/daughters (8), sister/brother (3) and sister-in-law (1). Controls informants were spouses (45), sons/daughters (4), and sister-in-law (1). Patients with MCI had a higher Charlson Index (2.71 ± 0.94) than controls (2.08 ± 1.16, $p = 0.03$, Student's *t* test).

No statistically significant differences among the groups were found in SWLS (Table 2). MCI patients had lower scores in MMSE and LM and higher scores in GDS compared to the other groups (Table 2).

The total scores of the QOL-AD questionnaire for MCI patients, fulfilled by themselves (MCI) and by their informants (MCI-informants), and for control participants, fulfilled by themselves (controls) and by their informants (controls-informants) are shown in Table 2. The between-subjects analysis showed that MCI patients had lower total QOL-AD scores than

Table 1. Study population demographic characteristics.

		MCI	MCI informants	Control	Control informants	
N		25	25	26	26	*p*-value
Age (years)	Mean (SD)	70.8 (6.2)	66.9 (9.5)	66.3 (10.8)	66.7 (9.9)	0.05*
Sex	Men/women	22/28	21/29	25/25	23/27	0.87[†]
Education (years)	Mean (SD)	10.7 (4.5)	11.1 (4.7)	9.0 (4.0)	9.7 (4.6)	0.08*

Notes: *One-way ANOVA.
[†]Chi-square test.

Table 2. Comparison of MMSE, LM, GDS, SWLS and QOL-AD scores in the study population.

		MCI	MCI informants	Control	Control informants	p-value	Statistical significance
MMSE	Mean (SD)	26.3 (2.1)	29.3 (1.7)	29.6 (0.6)	29.7 (0.6)	<0.001*	MCI < MCI-I, C, C-I
LM	Mean (SD)	7.5 (2.5)	17.5 (1.8)	16.8 (2.2)	17.6 (2.1)	<0.001*	MCI < MCI-I, C, C-I
GDS	Mean (SD)	4.8 (2.5)	2.1 (1.9)	2.3 (2.2)	2.0 (2.1)	<0.001*	MCI > MCI-I, C, C-I
SWSL	Mean (SD)	22.6 (6.8)	24.7 (6.1)	24.3 (4.9)	24.5 (5.3)	0.24*	NS
QOL-AD total	Mean (SD)	32.1 (6.9)	27.2 (6.7)	35.3 (4.9)	35.6 (4.9)	#	#

Notes: *One-way ANOVA followed by *post-hoc* Tukey's test if appropriate.
#Repeated measures ANOVA, globally MCI patients had lower QOL-AD scores than controls ($p < 0.001$), there was a significant difference between the subjects' own report and their informants' report in MCI patients ($p = 0.007$), see text. NS: not statistically significant; MCI-I: MCI patient informant; C: Control subject; C-I: Control subject informant.

Table 3. Scores in individual items of QOL-AD in MCI patients and control subjects, reported by themselves and by their informants.

	MCI	MCI informants	Control	Control informants	Statistical significance*
QOL-AD – physical health	2.22 (0.79)	1.98 (0.87)	2.44 (0.67)	2.38 (0.67)	
QOL-AD – energy	1.94 (0.91)	1.90 (0.89)	2.40 (0.73)	2.54 (0.71)	MCI < C
QOL-AD – mood	2.32 (0.79)	2.04 (0.90)	2.70 (0.68)	2.50 (0.65)	MCI < C
QOL-AD – living situation	2.58 (0.70)	2.50 (0.79)	2.68 (0.59)	2.54 (0.65)	
QOL-AD – memory	1.76 (0.89)	1.58 (0.73)	2.78 (0.98)	2.80 (0.93)	MCI < C
QOL-AD – family	2.98 (0.82)	2.46 (1.07)	3.24 (0.75)	3.30 (0.68)	MCI > MCI-I
QOL-AD – marriage	2.80 (0.78)	2.48 (0.93)	3.18 (0.60)	3.18 (0.60)	MCI < C
QOL-AD – friends	2.52 (0.70)	2.40 (0.95)	2.94 (0.55)	3.00 (0.45)	MCI < C
QOL-AD – self as a whole	2.32 (0.79)	1.96 (0.83)	2.54 (0.61)	2.62 (0.53)	MCI > MCI-I
QOL-AD – ability to do chores around the house	2.30 (0.87)	1.84 (0.91)	3.22 (0.65)	3.22 (0.79)	MCI > MCI-I MCI < C
QOL-AD – ability to do things for fun	2.02 (0.94)	2.00 (0.90)	2.66 (0.87)	2.56 (1.01)	MCI < C
QOL-AD – money	2.40 (0.86)	2.24 (0.74)	2.06 (0.65)	2.04 (0.64)	
QOL-AD – life as a whole	2.42 (0.84)	2.06 (0.82)	2.70 (0.58)	2.84 (0.47)	MCI > MCI-I

Notes: Scores are mean (SD).
*Comparison of scores of individual QOL-AD items with one-way ANOVA. Analysis of differences between MCI and control self-reports, and between MCI self-report and informant report, was performed with the *post-hoc* Dunnett test (MCI self-report was the reference group).
Significant differences are shown ($p < 0.05$).

controls ($p < 0.001$). The within-subjects analysis showed statistically significant differences between the subject's own report and their informant's report ($p = 0.025$). A significant interaction between the report of QoL (own report vs. informant's report) and group (MCI vs. control) was found ($p = 0.007$; repeated measures ANOVA; Table 2). In other words, the significant difference between the subjects' self report and their informants' report was driven by the MCI patients.

Since MCI patients had a lower total QOL-AD score than controls, we compared the individual QOL-AD items in both groups. Significantly lower individual QOL-AD item scores were observed in seven of the 13 items in MCI patients ('Energy', 'Humor', 'Memory', 'Marriage', 'Friends', 'Ability to do things for fun', and to do 'House chores') (Table 3).

Since the QoL-AD total score was higher in the report of MCI patients than in the opinion of their caregivers, we also compared in these patients the individual QoL-AD item self-report scores and

informant scores. The MCI patients' report was more favorable than the opinion of their informants for the items: 'Family', 'Hability to do house chores', 'Self as a whole', and 'Life as a whole' (Table 3).

Discussion

The main finding of the present study was that the QoL of MCI patients was decreased as compared to controls without cognitive impairment. Whereas the reports of controls and their informants were concordant, the QoL reported by patients with MCI was more favorable than the opinion of their informants.

It has been controversial whether the QoL is affected in patients with MCI. Two previous studies found no differences in QoL between MCI patients and healthy controls, using different instruments to evaluate QoL (Missotten et al., 2008; Ready et al., 2004). The first study used the Dementia QoL Scale (Brod, Stewart, Sands, & Walton, 1999), an instrument

applied to both the patient and the informant that assesses positive affect, negative affect, feelings of belonging, self-esteem, and sense of aesthetics, which are quite distinct from the concrete domains addressed in the QOL-AD scale (Table 3). The other study used the Alzheimer's Disease related QoL (Rabins, Kasper, Kleinman, Black, & Patrick, 1999), which reflects caregiver judgments about the patient's social interaction, awareness of self, feelings and mood, enjoyment of activities, and response to surroundings; and since it tackles rather basic behaviors of the patient, it may not be sensitive to early phases of cognitive decline. Still another study found in patients with MCI differences in one domain, psychological QoL, but not in other domains or in total score of the self-reported World Health Organization QoL scale (Muangpaisan et al., 2008).

The present study, using the QOL-AD scale, which allows appraisal of QoL in patients with cognitive decline both from the patient and the informant points of view, clearly shows that patients with MCI have a decrease in their QoL. This decrease involved several respects of QoL beyond cognition, namely social relationships, ability to enjoy himself/herself and mood. Although MCI patients had slightly higher scores on Charlson comorbidities index than control subjects, both groups scored at the same level of comorbidity, so this factor would not explain the difference of QOL-AD between MCI patients and controls.

An interesting finding of the present study is that the QoL reported by patients with MCI was more favorable than the opinion of their informants, whereas the reports of healthy controls and their informants were concordant. The tendency for informants to rate QoL lower than patients is consistent with what is observed in more advanced stages of cognitive decline, that is, dementia or Alzheimer's disease (Conde-Sala et al., 2009; Hurt et al., 2008; Ready et al., 2004; Thorgrimsen et al., 2003; Vogel et al., 2006). Although the MCI patients had more depressive symptoms, reflected by higher GDS scores, and previous studies have found a higher prevalence of depressive symptoms in patients with MCI (Solfrizzi et al., 2007), the presence of depressive symptoms could not explain the observed difference in the QoL reported by patients with MCI and their informants, since they would tend to worsen their perception of QoL, just the opposite of what was observed. On the other hand, their informants, who were also often their caregivers, were not more depressed than the healthy controls or their informants, thus ruling out that caregivers' depression would explain a more negative opinion about their patients' QoL. However, the possibility that informants, by being aware of the clinical status and memory complains of their patients, could overestimate small deficits cannot be excluded. The finding that the QoL reported by patients with MCI was better than the opinion of their informants is probably better explained by MCI patients being less aware of their cognitive and functional decline. In fact, some degree of anosognosia was previously described in patients with MCI (Galeone, Pappalardo, Chieffi, Iavarone, & Carlomagno, 2011). However, it should be noted that when scores in individual QOL-AD items were compared between MCI patients and their informants, the item 'Memory' showed no statistical difference, which suggests that patients with MCI were quite aware of their cognitive difficulties. On the other hand, patient scores were significantly higher for the item 'Ability to do chores around the house', which may reveal lack of insight about the functional decline. Differences in individual QOL-AD items may reflect not only distinct perceptions but also different expectations from the MCI patients and their informants (Carr, Gibson, & Robinson, 2001).

A few comments about the characterization of the MCI patients recruited in the present study are worthwhile. Although the MMSE scores in MCI patients were within the normal range, they were significantly lower than in the other groups, as found in previous studies (see, for instance, Nunes et al., 2010). The decrease in QoL found in MCI patients with QOL-AD was not paralleled by a corresponding decrease in satisfaction with life, as measured with the SWLS scale. This finding strengthens the idea that these instruments address distinct constructs.

Limitations of the present study must be recognized, in particular, the sample used for MCI group in this study consisted mainly of patients from a memory clinic, and the results may not be extended to general population.

In conclusion, the QoL was decreased in MCI patients as compared to controls without cognitive impairment. The QoL reported by patients with MCI was better than the opinion of their informants. QoL appears to be an important domain to be evaluated in studies in MCI, and possibly an interesting outcome measure for therapeutic interventions.

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