INSIGHT, COGNITION AND QUALITY OF LIFE IN ALZHEIMER'S DISEASE

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ABSTRACT

Background

The detrimental impact of dementia upon patient health related quality of life (HRQL) is well established as is the importance of improving HRQL. However, relatively little is known about the natural history of HRQL in dementia and those factors influencing it. This limited knowledge potentially restricts the evaluation of the efficacy of interventions designed to improve HRQL. One such area concerns the relationship between HRQL and patient insight. It remains unclear what impact, if any, impaired insight has upon a patient's HRQL. The present study aimed to investigate the relationship between insight and HRQL in a sample of patients with Alzheimer's disease (AD) and their carers.

Methods

256 patients with AD were recruited as part of AddNeuroMed, a multi-centre European AD biomarkers study. Of these 174 completed a quality of life measure in addition to a comprehensive battery of clinical and neuropsychological assessments.

Results

Insight was found to be differentially related to patient perceptions of HRQL in mild and moderate dementia. Within moderate dementia impaired insight was associated with better perceived HRQL. Conversely cognition, but not insight, was associated with impaired HRQL in mild dementia. Insight was not found to be associated with carer perceptions of patient HRQL.

Conclusion

Impairment of insight is associated with better HRQL in moderate dementia. This finding has implications for interventions which focus on increasing patient awareness and orientation as impairment of insight appears to have a positive impact upon HRQL.

Introduction

The past ten years have seen increasing attention paid to the investigation of Health Related Quality of Life (HRQL) in dementia.[1] The behavioural, and psychological symptoms experienced by patients with dementia have a profoundly negative impact upon quality of life in people with dementia.[2-9] Improving quality of life for people with dementia has become a priority in dementia care and HRQL has been frequently suggested as an indicator of the effectiveness of both psychosocial and pharmacological interventions.[10,11] Although increasing attention is being paid to HRQL in dementia we remain largely ignorant about who suffers most loss of HRQL and the factors influencing this.[12]

We need to understand what determines good and bad HRQL in dementia if we are to develop and evaluate interventions to improve HRQL. A better understanding of factors influencing HRQL in dementia might enable us to identify those most at risk of declining HRQL so allowing monitoring and provision of appropriate treatment when necessary.

One such area in need of further investigation is the relationship between HRQL and insight. It seems intuitive that being aware of decline might adversely impact on HRQL, and relatives may resist clinicians discussing diagnosis on the grounds that this might negatively impact on the patient. However it remains unclear what (if any) is the effect of a person with dementia's insight into their condition has on their HRQL. Investigations into the relationship between patient insight and HRQL have produced equivocal results,[13,14] albeit with relatively small samples. Ready et al. [14] found no relationship between clinician ratings of insight and either patient or carer measures of HRQL in a sample of 26 people with Alzheimer's disease (AD). Consistent with Ready et al.'s study, HRQL was not found to differ between patients with impaired insight and those with full awareness in a sample of 48 people with mild AD.[13] However when the relationship between patient and carer measures of HRQL was examined, scores were found to correlate within the full insight sample but not in those with impaired insight. Impairment of insight may have led people with dementia to perceive their HRQL more positively than it was perceived by their carer, as suggested by the lack of association between the two scores.

We therefore sought to examine the relationships between HRQL and insight in a sample of people with Alzheimer's disease and their carers. We explored how these relationships varied with degree of cognitive impairment in an attempt to determine the natural course of the relationship between insight and HRQL with progression of dementia. We hypothesised that people with dementia with impaired insight would perceive their HRQL to be better than those with full insight.

Methods

Two hundred and fifty six patients with mild to moderate Alzheimer's disease were recruited as part of AddNeuroMed, a multi-centre European AD biomarkers study.[15] The six participating clinical centres included University Hospitals in Kuopio, Perugia, Lodz, Thessaloniki, Toulouse and London. Subjects were people with dementia who attended local dementia clinics and had received a diagnosis of AD.

Inclusion criteria were: possible or probable AD according to the NINCDS-ARDA and DSM IV; a MMSE score of between 12-30; and age 65 years or above. Patients with significant neurological or psychiatric illness other than AD or any significant unstable systematic illness or organ failure were not included in the study.

A comprehensive semi-structured evaluation was conducted with all patients and caregivers assessing cognition (Mini-Mental State Examination (MMSE),[16] Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog),[17] function (Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory (ADCS-ADL),[18] behavioural and psychological symptoms (Neuropsychiatric Inventory (NPI)[19] and health related quality of life (DEMQOL)[20,21] (see table 1 for descriptive data). The DEMQOL consists of a 28-item interviewer-administered questionnaire that is self-reported by the person with dementia (DEMQOL) and a 31-item interviewer-administered questionnaire that is proxy-reported by a caregiver (DEMQOL-Proxy). For all assessments a higher score indicated better functioning with the exception of the ADAS-Cog where a higher score suggested poorer cognitive function. A total of 174 patients had either a DEMQOL-Proxy score or a self-rated DEMQOL score or both (155 proxy, 162 self).

Two measures of patient insight were employed. The first was a dichotomous researcher rating of patient insight; patients were rated as having good or partial/little insight (rater scored insight). The second measure of insight was based on the patient's response to the question 'Do you have problems with memory or thinking?' Possible responses included 'yes', 'no' and 'don't know' (self scored insight). These questions were derived from the Clinical Dementia Rating Scale worksheet. [22]

The study was approved by the South London and Maudsley NHS Foundation Trust ethics committee and appropriate ethical approval was gained in all other participating countries.

Results

The final dataset included 174 patients with an MMSE score between 12 and 30. In order to examine the consistency of relationships between HRQL and insight with dementia stage, the sample was stratified by MMSE score to produce two groups: mild (MMSE score between 21 and 30) and moderate dementia (MMSE score between 12 and 20). All further cognitive analyses used scores from the ADAS-Cog which provides a more detailed assessment of cognition than the MMSE. The sample demographic data are shown in table 1 along with mean MMSE, ADAS-Cog and DEMQOL scores.

Table 1. Sample demographic data and MMSE, ADAS-Cog and patient and proxy DEMQOL scores

	N	Age (sd)	M:F	Education Years (sd)	MMSE (sd)	ADAS-Cog (sd)	Duration of illness (sd)	DEMQOL Patient	DEMQOL Proxy
All	174	77.2 (6.5)	67:107	8.4 (4.1)	20.6 (4.9)	24.8 (9.9)	4.1 (3.1)	90.8 (15.7)	97.8 (13.7)
MMSE 12-20	79	78.5 (6.5)	30:49	7.3 (3.8)	16.1 (2.5)	30.9 (8.2)	4.3 (3.1)	92.0 (16.5)	98.9 (11.7)
MMSE 21-30	95	75.9 (6.3)	37:58	9.2 (4.1)	24.5 (2.4)	19.5 (8.0)	3.9 (3.2)	89.9 (14.3)	97.2 (15.0)

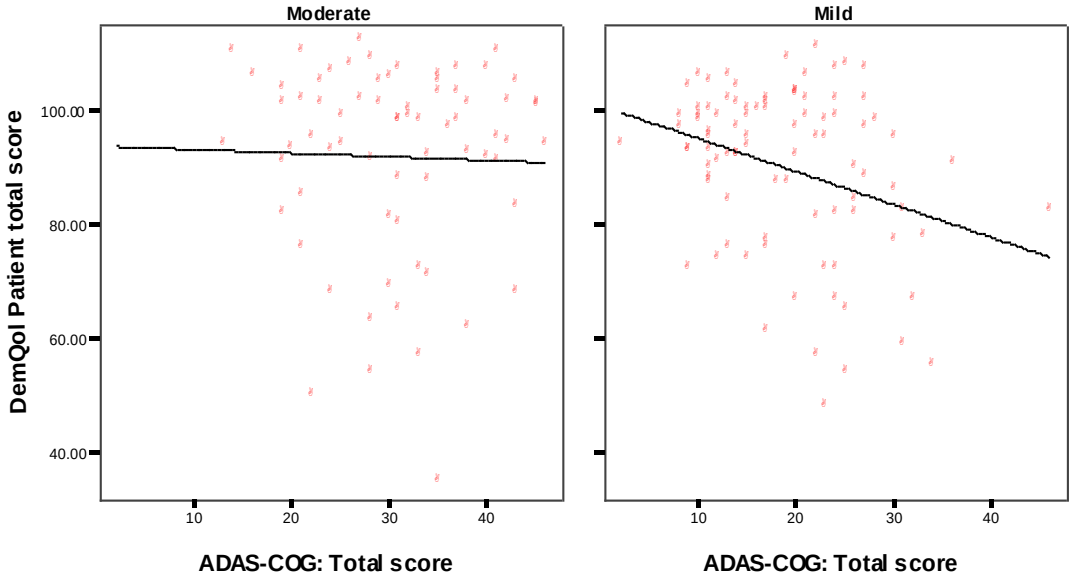
We first established that a range of demographic and clinical characteristics were not associated with HRQL and hence were not acting as confounders in subsequent analyses. We found no association between HRQL and age, marital status, years of education, duration of illness, activities of daily living and carer characteristics, none of which were statistically significant ($p<0.05$).

Cognition and HRQL

Previous studies of HRQL consistently find little impact of cognition *per se* on HRQL,[12] we confirmed this finding in our dataset as no significant correlation was found between cognition and HRQL in the sample as a whole (Pearson correlation between ADAS-Cog score and DEMQOL r = -.07, p = .41, DEMQOL-Proxy r = -.14, p = .08).

However, Alzheimer's disease is a chronic disorder and the relationship between HRQL and symptoms may change as the disease progresses. To test this relationship further, correlations between ADAS-Cog scores and HRQL scores within the mild and moderate dementia samples were calculated separately. No significant correlations were found within the moderate sample (DEMQOL r = -0.001, p =0 .995, DEMQOL-Proxy r = -0.011, p = 0.928), however ADAS-Cog scores were significantly correlated with HRQL in the mild sample (DEMQOL r = -0.27, p = 0.010, DEMQOL-Proxy r = -0.354, p = 0.001). The relationships between cognition and HRQL are presented in figure 1.

Figure 1. Scatterplot of ADAS-Cog and Patient DEMQOL Scores by MMSE Group



Behavioural and Psychological Symptoms and HRQL

Previous research has shown that behavioural and psychological symptoms such as depression, irritability and agitation have a profound negative impact on HRQL.[12] We confirmed this finding in this large cross-European study. The NPI was used as a measure of behavioural and psychological symptoms and, as predicted, total NPI scores strongly correlated with both patient and carer DEMQOL scores (DEMQOL: r = -0.190, p = 0.016, DEMQOL-Proxy: r = -0.244, p = 0.002). The presence of behavioural and psychological symptoms was associated with significantly poorer HRQL. We then sought to determine which sets of behavioural and psychological symptoms impacted most on HRQL. Moderately strong relationships were found between depression and DEMQOL score (r = -0.425, p <0.001), and between depression and anxiety and DEMQOL-Proxy scores (depression: r = -0.391, p <0.001, anxiety: r = -0.396, p <0.001).

Correlations between NPI scores and HRQL were examined within the mild and moderate dementia samples to explore the consistency of the relationships between NPI scores and

HRQL across dementia stages. Within the mild sample hallucinations were highly correlated with self-report (r = -0.314, p =0.002) and proxy-reports (r = -0.384, p 0.001). Depression and anxiety were again found to correlate moderately strongly with DEMQOL-Proxy score (depression: r = -0.341, p = 0.002, anxiety: r = -0.476, p <0.001). Within the moderate sample DEMQOL was strongly correlated with depression (r = -0.580, p <0.001) while irritability and depression were correlated with DEMQOL-Proxy scores (r = -0.376, p = 0.001, r = -0.486, p <0.001 respectively). For both mild and moderate dementia, then, we find strong correlations between behavioural and psychological symptoms and HRQL.

Insight, cognition and HRQL

We then investigated the relationship between insight and both HRQL and cognition. We hypothesised that HRQL would be impaired in those with good insight and, as a secondary hypothesis, that those with more severe cognitive impairment would have the least insight.

Table 2 Quality of Life and Cognition by Insight Group

	Self Scored Insight			**Rater Scored Insight**		
	Good Insight	*Impaired Insight*	**T-Test**	*Good Insight*	*Impaired Insight*	**T-Test**
12-20 MMSE						
No	59	19		24	54	
%	76.0%	24.0%		30.8%	69.2%	
DEMQOL	96.7	99	$t_{(68)} = 2.160$ $p = 0.010$	84.7	95.8	$t_{(68)}=-2.741$ $p = 0.008$
DEMQOL-Proxy	89.6	105.9	$t_{(68)}=2.808$ $p = 0.006$	95.1	100.5	$t_{(68)}=-1.842$ $p = 0.070$
ADAS COG	30.4	32.5	$t_{(76)}= .989$ $p = 0.327$	27.6	32.3	$t_{(76)}=-2.423$ $p = 0.018$
21-30 MMSE						
No	74	20		54	40	
%	77.9%	21.1%		57.4%	42.6%	
DEMQOL	89	93	$t_{(88)} =1.056$ $p = 0.294$	88.4	92.3	$t_{(88)}=-1.270$ $p = 0.207$
DEMQOL-Proxy	96.9	97.8	$t_{(80)}=.230$ $p = 0.818$	96.7	97.6	$t_{(80)}=-.269$ $p = 0.789$
ADAS COG	18.6	22.9	$t_{(92)}= 2.155$ $p = 0.034$	17	22.8	$t_{(92)}=-3.676$ $p < 0.001$
Total sample						
No	133	39		79	94	
%	77.3%	22.7%		45.7%	54.3%	
DEMQOL	89.3	96.1	$t_{(159)} = 2.406$ $p = 0.017$	87.4	94.3	$t_{(171)}=4.724$ $p < 0.001$
DEMQOL-Proxy	96.6	101.4	$t_{(150)}=1.726$ $p = 0.086$	95.9	99.3	$t_{(151)}=-1.550$ $p = 0.123$
ADAS COG	24	27.5	$t_{(170)}=2.102$ $p = 0.037$	20.6	28.2	$t_{(171)}=-5.452$ $p < 0.001$

As shown in table 2, and in agreement with our hypothesis, HRQL was rated as higher in those with impaired insight, although only in the moderate dementia group (a trend for proxy rating in the rater scored insight group, but significant for all other analyses). HRQL did not differ according to insight in those with mild dementia.

In order to investigate whether impairment of patient insight was associated with worse cognition, ADAS-Cog scores were compared between insight groups using independent t-tests. Those with impaired insight had more severe cognitive deficit in both moderate and mild groups (non significant difference for moderate dementia and self scored insight but highly significant for all other comparisons).

Multivariate Analyses

Thus far we have established that cognition, behavioural and psychological symptoms, and insight are all associated with HRQL in dementia. In order to determine the relative contributions of each of these variables to the explanation of variance in HRQL, a series of regression analyses were performed. Separate regressions were performed for DEMQOL and DEMQOL-Proxy scores within each MMSE group. Separate regressions were performed using the rater scored and self scored insight measures in order to avoid the problem of multi-collinearity. The adjusted R squared and standardised regression weights are shown in tables 3 and 4.

Table 3.Regression Models of Factors Predicting Patient DEMQOL scores

DEMQOL (MMSE 12-20)	Beta coefficient	R square	Adjusted R square	Significance
		0.365	0.336	<0.001
ADAS-Cog	-0.079 (p=0.438)			
NPI depression score	-0.505 (p<0.000)			
Rater scored insight	0.245 (p=0.022)			
DEMQOL (MMSE 21-30)				
		0.231	0.204	<0.001
ADAS-Cog	-0.403 (p<0.001)			
NPI hallucinations score	-0.255 (p=0.009)			
Rater scored insight	0.243 (p=0.020)			
DEMQOL (MMSE 12-20)	Beta coefficient	R square	Adjusted R square	Significance
		0.355	0.325	<0.001
ADAS-Cog	-0.051 (p=0.616)			
NPI depression score	-0.535 (p<0.000)			
Self scored insight	-0.211 (p=0.040)			
DEMQOL (MMSE 21-30)				
		0.218	0.109	<0.001
ADAS-Cog	-0.365 (p<0.001)			
NPI hallucinations score	-0.289 (p=0.003)			
Self scored insight	-0.203 (p=0.042)			

Depression and insight significantly predicted DEMQOL scores in the moderate dementia group but cognition was not found to predict HRQL. Both cognition and insight predicted patient HRQL in mild dementia along with hallucinations. The relationship between HRQL and insight in the 21-30 MMSE group was unexpected as this relationship was not present within the bivariate analyses. However there is a strong relationship between insight and cognition in this sample. In order to test whether the relationship seen between insight and HRQL in the 21-30 MMSE group was a product of the relationship between cognition and insight, insight was entered into stepwise regression models alone in the first step. Insight significantly predicted HRQL in the 12-20 MMSE group only, insight did not significantly predict HRQL in the 21-30 MMSE sample for either measures of insight.

Table 4. Regression Models of Factors Predicting Proxy DEMQOL scores

DEMQOL-Proxy (MMSE 12-20)	Beta coefficient	R square	Adjusted R square	Significance
		0.191	0.141	0.008
ADAS-Cog	-0.055 (p=0.641)			
NPI depression score	-0.292 (p=0.017)			
NPI anxiety score	-0.166 (p=0.160)			
Rater Scored insight	0.184 (p=0.131)			
DEMQOL-Proxy (MMSE 21-30)				
		0.443	0.406	<0.001
ADAS-Cog	-0.189 (p<0.001)			
NPI hallucinations score	-0.126 (p=0.184)			
NPI depression score	-0.270 (p=0.003)			
NPI anxiety score	-0.386 (p<0.001)			
Rater Scored insight	0.119 (p=0.211)			
DEMQOL-Proxy (MMSE 12-20)	Beta coefficient	R square	Adjusted R square	Significance
		0.230	0.182	0.002
ADAS-Cog	-0.013 (p=0.907)			
NPI depression score	-0.298 (p=0.011)			
NPI anxiety score	-0.137 (p=0.232)			
Self Scored insight	-0.298 (p=0.020)			
DEMQOL-Proxy (MMSE 21-30)				
		0.426	0.388	<0.001
ADAS-Cog	-0.313 (p=0.001)			
NPI depression score	-0.271 (p=0.003)			
NPI hallucinations score	-0.133 (p=0.166)			
NPI anxiety score	-0.385 (p<0.001)			
Self Scored insight	-0.090 (p=0.316)			

Consistent with the patient-DEMQOL models, cognition was found to predict DEMQOL-Proxy scores in the 21-30 MMSE sample only. NPI items significantly predicted HRQL in all models. Self Scored insight was found to predict DEMQOL-Proxy scores in the 12-20 MMSE group only.

Discussion

The present study aimed to investigate whether insight was associated with self and proxy-reports of HRQL in Alzheimer's disease. Few studies have undertaken such a large scale investigation of insight and HRQL using two measures of insight. We find that in moderate dementia only, impaired insight is associated with better HRQL but that in mild dementia there is no such association. In contrast, impaired cognition negatively impacts on HRQL only in those with mild dementia. Behavioural symptoms on the other hand have a negative impact on HRQL in both mild and moderate dementia.

Summary of findings

In line with previous research, demographic factors were not associated with HRQL and the presence of behavioural and psychological symptoms were associated with poorer HRQL;[12]

in both moderate and mild dementia. Lower cognition was correlated with lower HRQL in mild but not moderate dementia suggesting that declining cognition does not necessarily lead to reduced HRQL. The lack of relationship between cognition and HRQL in moderate dementia suggests either that patients are less aware of the cognitive difficulties they experience or that they have adapted and 'regraded' their expectations, accommodating to impairment. By changing goals and expectations patients may avoid distress produced by failure to perform tasks and activities previously considered achievable.[23]

Insight and cognition are clearly related in AD, with impaired insight associated with poorer cognition, however in moderate dementia insight alone impacts on quality of life, whilst in mild dementia cognition impacts on quality of life. This finding is consistent with previous research in mild AD which failed to find any association between insight and HRQL.[14]

Overall the findings suggest that insight plays a complex role in evaluations of HRQL in dementia. People with moderately severe dementia and impaired insight into their condition showed a tendency to perceive their quality of life as better. For those with mild dementia, and therefore potentially higher levels of insight, this protective effect was not observed.

Implications

The finding that impaired insight is associated with better HRQL suggests that impairment of insight may actually be protective for the person with dementia. Relatives often say as much. This raises questions about the management which should be provided for patients who lack awareness. Re-orientating patients to their situation through the use of therapies such as reality orientation, which repeatedly require the patient to acknowledge problems, may have the effect of increasing awareness and therefore reducing HRQL. The effect of other therapies aimed at improving cognition such as cognitive stimulation [24] is of interest as a form of intervention potentially benefitting HRQL in mild dementia through improved cognition

The observed relationship between cognition and quality of life in mild dementia highlights the need for monitoring of newly diagnosed patients for decline in HRQL with deteriorating cognition. Monitoring will allow appropriate intervention in order to improve HRQL. Helping patients with mild dementia to adjust their goals and expectations, accommodating their cognitive impairment, may improve quality of life for these patients. When a person experiences declines in their cognition their previous goals may become unrealistic, the gap between their present state and desired state widens reducing quality of life. Revising goals to be more achievable may help to improve quality of life [25].

The results also have implications for research into health-related quality of life. When conducting research investigating the effectiveness of interventions on HRQL in dementia it may well be useful to measure insight.

Limitations

The present study has limitations which must be taken into consideration. First, the single item approach to measuring insight employed in the present study was relatively simplistic however both measures produced similar results providing validity for the measures. Second, this is a cross-sectional study and we cannot draw any conclusions regarding causality. A longitudinal investigation of HRQL and insight in dementia would be helpful to chart the natural history of HRQL in dementia and allow causal relationships to be investigated. Finally, the study only included patients with an MMSE score of 12 and above. No conclusions can therefore be drawn about insight and HRQL in people with severe cognitive impairment in dementia.

Conclusions

The findings from this study suggest that insight is an important determinant of HRQL for people with moderate dementia. This finding validates the anecdotal reports of relatives and suggests that lack of insight may act as a protective mechanism. Insight was found to have no impact on HRQL in mild dementia suggesting that clinicians should not be worried about discussing diagnosis and plans for the future with patients. Behavioural and psychological symptoms were found to negatively impact on HRQL at all stages suggesting that clinicians should focus on alleviating these symptoms to improve quality of life.

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