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Health related quality of life, cognitive performance, and incident dementia in a community based elderly cohort.

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Abstract

Background: We hypothesized that higher quality of life would be associated with better cognitive function and a reduced risk of incident all cause dementia and Alzheimer's disease (AD) in older adults.

Methods: Participants included 1183 older adults with an average age of 78.2 (SD=5.3) from Einstein Aging Study (EAS). The Short-Form Health Survey (SF-36) was used to measure HRQoL. We investigated baseline associations between the cognitive domains of memory, executive function, and general fluid ability with eight subscales of the SF-36 (physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, social functioning, role limitations due to emotional problems, vitality, and general mental health) and the two component summary scores of Physical Component Summary (PCS) and Mental Component Summary (MCS). Next, we used Cox proportional hazard models to assess the predictive validity of HRQoL subscales for the onset of incident dementia and incident AD.

Results: At baseline, higher scores (better HRQoL) on MCS and its 4 subscales (social functioning, role limitations due to emotional problems, vitality, and general mental health) were associated with higher performance on both memory and executive function domains. Higher scores in role limitation due to physical problems, role limitation due to emotional problems and general mental health subscales were associated with reduced risk of incident dementia. Higher MCS, but not PCS, predicted a reduced incident of all-cause dementia and AD.

Conclusions: These findings suggest that diminution of HRQoL precedes the onset of diagnosable dementia and may be useful in the prediction of dementia onset.

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Keywords

Health Related Quality of Life; SF-36; Physical Health; Mental Health; Incident Dementia; Alzheimer's Disease; Cognitive Function; Memory; Executive Function

INTRODUCTION

Health-related quality of life (HRQoL) is generally defined as the subjective value assigned to the duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, or treatment.[1, 2] Prior studies have suggested that with all other influences controlled, aging per se does not influence quality of life negatively; rather a long period of good quality of life is possible.[3] Therefore, the maintenance and improvement of quality of life should be included among clinical management goals in older adults.

Prior research has suggested links between cognitive performance and HRQoL in older adults. Cognitive impairment might negatively affect different dimensions of HRQoL. For example, diminution in verbal abilities may interfere with the maintenance of social role function;[4] executive impairment may interfere planning and sequencing physical activates,[5] deficits in attention may interfere with daily activities such as bathing, and personal hygiene, [6] and awareness of cognitive dysfunction may cause depression altering indicators of mental health related quality of life.[7] In some cases, individuals not aware of their cognitive dysfunction may over-rate their functional status and HRQoL.[8] Two review papers reported inconsistent findings in this regard: Mitchell et al.[9] indicated that cognitive impairment may affect quality of life dimensions in patients with neurological disease; while Banerjee et al.[10] reported that there is no convincing evidence of association between cognitive impairment and HRQOL in older adults. There is strong evidence that cognitive decline and neurodegenerative disease such as dementia, negatively affect HRQoL.[10] Yet the long-term association between HRQoL domains and incident dementia or Alzheimer's disease is not well stablished.

The Einstein Aging Study (EAS) includes a community-based sample of older adults with prospective data on HRQoL and cognitive function. In this study, initially we assessed the association between HRQoL subscales, as measured by the SF-36 questionnaire, and three cognitive domains (episodic memory, executive function and general fluid ability) derived from previous principal component analysis.[11] Subsequently, we explored the associations between HRQoL subscales, and the risk of incident all-cause dementia and Alzheimer's disease (AD). We hypothesized that higher scores on HRQoL, specifically in mental health subscale, would be associated with better cognitive function at cross-section, and decreased incident dementia during the longitudinal follow-up.

METHODS

Study population

The EAS includes a systematic sample of older adults residing in a Bronx, NY. Participants were systematically sampled from Medicare or Voter Registration Roles by telephone

screening. Eligible participants are age of 70 years or older, English speaking, and free of dementia at the initial study visit. Comparison with U.S. Census data indicates that the cohort is representative of the Bronx County community with respect to sex, race/ethnicity and educational level at the time of enrollment. Participants undergo annual assessments including clinical evaluations, a neuropsychological battery, psychosocial measures, medical histories, demographics, standardized assessments of activities of daily living, and self- and informant reports of memory and cognitive complaints. Study details are described elsewhere.[12]

This analysis included data from 1183 EAS participants, enrolled between February 1994 and February 2016, who completed the SF-36 questionnaire at baseline and had at least one subsequent annual follow-up. Participants who met criteria for dementia at baseline were excluded from this study.

Standard protocol approvals, registrations, and patient consents.

Written informed consent was obtained from all participants at study entry. Study protocols were approved by the Albert Einstein College of Medicine institutional review board.

Clinical information and measurement of risk factors

Trained research assistants used structured questionnaires to obtain demographic information (age, sex, race/ethnicity and years of education) as well as medical history at each annual visit. Using baseline medical history, we calculated a medical comorbidity index score (ranging from 0 to 9) from dichotomous self-report of having ever been diagnosed (present vs absent) with hypertension, diabetes, stroke, myocardial infarction, angina, congestive heart failure, Parkinson’s disease, rheumatoid arthritis, and chronic obstructive pulmonary disease as previously described.[13]

Health-related quality of life assessment—The Medical Outcomes Study (MOS) 36-Item Short Form Health Survey (SF-36)[14, 15] is a well-vali ted rating scale that measures health-related quality of life in patients suffering from different diseases and in healthy persons. Previous studies have shown that the SF-36 is suitable, valid, and reliable for use with the elderly population with normal cognition or with mild cognitive impairment (MCI).[16, 17] The taxonomy of items and concepts underlying the construction of the SF-36 scales and summary are discussed in previous studies.[18] In summary, the taxonomy has three levels: (1) thirty-six items, (2) eight subscales that aggregate 2–10 items each: physical functioning, role limitations due to physical problems (role-physical), bodily pain, general health perception, vitality, social functioning, role limitations due to emotional problems (role-emotional), and (3) two summary measures that aggregate scales: physical component summary (PCS) and mental component summary (MCS). All but one of the 36 items (self-reported health transition) are used to score the eight SF-36 scales (after linear transformation, each subscale scores range from 0 to 100, where 100 denotes the best health). The eight scales are hypothesized to form two distinct higher ordered clusters according to the physical and mental health variance that they have in common. Component summary scores are calculated based on USA-specific norms. Higher scores in all subscales and summary components represent better HRQoL in that domain.

Assessment of cognitive function—To reduce the number of comparisons (Type I error) and to increase reliability, many groups including our own combine individual neurocognitive tests to generate summary measures of cognitive domains.[19, 20] For the purpose of this study, based on a within sample principal component analysis (PCA), the EAS cognitive battery was summarized into 3 different domains: *I) Memory domain*, comprised of the free recall scores and total recall scores from the Free and Cued Selective Reminding Test (FCSRT),[21] the total score from a test of category fluency, also known as semantic fluency,[22] and The Logical Memory I subtest from the Wechsler Memory Scale-Revised (WMS-R),[23]; *II) Executive function domain*, comprised of The Trail Making Test (TMT) part B,[24] and two WAIS-IV subtests,[25] the Digit Symbol Test and Block Design; *III) General fluid ability domain*, comprised of Vocabulary, Information and Digit Span from the WAIS-IV,[25] and the Controlled Oral Word Fluency Test (FAS),[26] and the Boston Naming Test.[27] Details of the PCA analysis and tests used for it has been described previously.[28]

Dementia diagnosis—Dementia was diagnosed according to standardized criteria from the Diagnostic and Statistical Manual, fourth edition (DSM-IV) and required impairment in memory plus at least one additional cognitive domain, accompanied by evidence of decline from a previous level of functioning [31]. A licensed neuropsychologist used normative data to determine whether impairment existed in any of the cognitive domains [32]. A physician independently interviewed and examined each participant, completed the Clinical Dementia Rating (CDR) scale,[29] and documented a clinical impression of whether dementia was present [33–35]. Final diagnostic determination was made at consensus case conferences attended by a licensed clinical neuropsychologist and a board-certified neurologist. Diagnosis of Alzheimer disease was determined for individuals with dementia who met clinical criteria for probable or possible disease established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association.[30]

Statistical Methods—All other statistical analyses were conducted using SPSS, version 25 (Chicago, IL: SPSS Inc.). The effect of baseline HRQoL on the risk of incident dementia was evaluated using Cox proportional hazards regression analysis, and estimated hazard ratios (HR) with 95 percent confidence intervals are reported. The time to event was defined as the time from the baseline visit, to the visit at which dementia was first diagnosed or to the date of last follow-up. All models include age at enrollment, sex, race, educational level, and chronic medical comorbidity as covariates. Separate Cox proportional hazards models were used to evaluate the association between incident dementia and seven sub-scales of the SF-36 (physical functioning, role-physical, social functioning, role-emotional, vitality, mental health, and general health perceptions) and two summary scores (PCS and MCS). Hazard ratios were calculated for each point change representing one standard deviation change in each subscale measure or component score. The proportional hazards assumptions for all models were adequately met according to methods based on scaled Schoenfeld residuals.[31] In order to prevent the possibility of type-I error, a Sidak correction factor [28] with an adjusted p value of 0.005 was used throughout the analysis (α=0.05, with 8 total subscales and 2 summary scores).

RESULTS

Demographic characteristics

The study included 1183 individuals, 38% of which were males. Mean age at baseline was 78.3 years (SD=5.3). Participants were followed on average for 4.6years (SD=3.5, Range=0.84–17.2 years), during which 127 individuals developed dementia. Of the 127 individuals with incident dementia, 105 met criteria for probable or possible AD. The group who developed dementia were on average older ($t=4.8$, $p<0.001$) but did not differ in sex, race, and education. Table 1 summarizes baseline characteristics for individuals who at final assessment developed dementia and for those who remained dementia free.

Associations between baseline HRQoL and cognitive function domains

Initially, we evaluated the association between cognitive function domains and HRQoL subscales at baseline (table 2). In models adjusted for age, gender, race, education, and medical comorbidity index, there was a significant positive association among all 4 mental subscales of SF-36 (social functioning, role-emotional, vitality, and general mental health) with both the memory and the cognitive function domains. The general health subscale was the only physical subscale of SF-36 to show a significant association with performance on executive function domain ($\beta=0.12$, $p<0.001$). General mental health was the only subscale significantly associated with performance on general fluid ability domain ($\beta=0.10$, $p<0.001$). Subsequently, we investigated the association between PCS and MCS, and cognitive function domains (table 3). Higher scores on MCS was associated with higher performance in memory ($\beta=0.11$, $p<0.001$) and executive function ($\beta=0.10$, $p<0.001$) domains. There was no association between PCS and any of cognitive function domains.

HRQoL and incidence of all-cause dementia and Alzheimer's dementia

Table 4 summarizes the Cox-proportional hazard models testing associations between SF-36 sub-scales and either incident all-cause dementia or incident AD. Models revealed that after controlling for demographics such as age, gender, education, race, and medical comorbidity, higher HRQoL based on subscales of role-physical ($HR=0.73$, $p<0.001$), role-emotional ($HR=0.80$, $p<0.001$), and mental health ($HR=0.78$, $p=0.003$) were associated with decreased risk of incident all-cause dementia. Repeating Cox proportional hazard models for prediction of AD as the outcome, yielded similar results (table 4).

Subsequently, we looked at the association of component summaries and incident dementia (table 5). Models showed that higher MCS scores (i.e. better mental health QoL) was associated with lower incident of all-cause dementia ($HR=0.79$, $p=0.003$) and AD ($HR=0.81$, $p=0.004$). There was no association between PCS and incident dementia or AD.

DISCUSSION

In this study, we showed that 1) at cross-section, there is a direct association primarily between mental health subscales of HRQoL (social functioning, role-emotional, vitality and general mental health) with memory and executive function domains in non-demented older adults; 2) higher scores on MCS (i.e. better mental health related quality of life) were

associated with higher performance on both memory and executive function domains; 3) during the longitudinal follow-up, lower baseline scores in specific subscales of role-physical, role-emotional and mental health were associated with increased incidence in both all-cause dementia and AD; and 4) there was a higher risk of dementia and AD in older adults with lower MCS scores, while the association between PCS and incident dementia or AD was not significant. Of note, in a previous study in the same population, we looked at the association between bodily pain *items* (questions on *pain intensity* and *pain interference*) from the SF-36 subscales, and we showed that higher pain interference, but not pain interference, has a significant association with incident dementia.[32]

The eight subscales of SF-36 are hypothesized to form two distinct higher ordered clusters, according to the physical and mental health variance that they have in common.[18] Factor-analytic studies have confirmed physical and mental health factors that account for 80–85% of the reliable variance in the eight scales in the US general population. The mental component correlates most highly with the mental health, role-emotional, and social functioning subscales, which also contribute most to the scoring of the MCS measure.[17] Considering the association between all subscales of Mental Health with memory and executive function domains at baseline, and strong association between role-emotional and general mental health subscales with incident dementia, the association between MCS and baseline memory and executive function, as well as incident dementia, was expected.

Despite the well documented association of decline in mobility and physical activity and incident dementia in older adults,[33, 34] in our study none of the physical component subscales (or PCS) were associated with memory function at baseline. In addition, aside from the role-physical subscale, none of the other physical component subscales were associated with higher risk of incident dementia. This inconsistency might be partially due to the fact that, in general, mental health problems occur earlier in the course of pathological aging and has higher association with change in rate of cognitive decline.[35] One other possibility is that participants in earlier stages of cognitive decline might recognize, and therefore report, the mental health issues earlier than physical limitations. Considering our findings, individuals with low HRQoL (specially when those with lower subjective mental health related QoL), might benefit from periodic cognitive assessments as they are at higher risk for cognitive decline and incident dementia.

AD and other types of dementia are among the most important contributors to disability in the elderly.[36] However, there is no effective preventive method or therapeutic option for them. Therefore, interventions that might delay the onset of dementia through modifications in risk factors are of particular importance. Prior studies have indicated that socially and mentally stimulating activity, as well as having a large social network may reduce risk of dementia.[37, 38] In addition, it has been shown that enhancing emotional involvement at home and community might positively affect cognitive function and QoL.[39] Similarly, there is strong evidence that interventions aiming to improve physical and general mental health might prevent or delay incident dementia.[33, 40] Our results emphasize the importance of targeting these HRQoL domains to improve general health, quality of life and potentially delaying dementia onset in susceptible populations.

The main strength of this study was using of a large community-based sample of older adults spanning a 17-year period of follow-up. However, a few limitations should be noted. The SF-36, similar to other HRQoL tests, is a self-reported and retrospective test evaluating the HRQoL over a 1-month period and might not be a true representation of HRQoL over a longer period of time. One solution to this issue in future studies is to prospectively collect information about daily quality of life over the course of weeks or months. Furthermore, our results may not be generalizable to older adults who were not qualified for this study due to health-related limitations such as individuals living at nursing homes or hospitals.

In conclusion, our study of community-based older adults demonstrates that poorer HRQoL is specific domains such as role-physical, social-functioning and general mental health are independent predictor of incident AD and all-cause dementia. Individuals with lower HRQoL in these domains, might need higher attention and care for the purpose of maintenance and improvement of quality of life.

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Table 1.

Baseline demographic variables in the entire sample, and comparison of participants based on dementia status at last follow-up date.

	Total sample, (N=1183)	Remained free of dementia (N=1056)	Developed dementia (N=127)	p-value
Women, N (%)	729 (61.6)	644 (61.0)	85 (66.9)	0.044
Race, White, N (%)	779 (65.8)	697 (66.0)	82 (64.6)	0.560
Age, years (SD)	78.2 (5.3)	78.0 (5.2)	80.4 (5.4)	0.006
Education, y, mean (SD)	13.9 (3.5)	13.9 (3.5)	13.6 (3.5)	0.079
Follow-up time, y, mean (SD)	4.6 (3.5)	4.6 (3.6)	4.3 (3.4)	0.087
SF-36 subscale scores, mean (SD)				
Physical functioning	73.5 (23.2)	73.5 (23.2)	73.7 (22.9)	0.066
Role-physical	81.7 (34.9)	82.6 (34.2)	74.2 (40.2)	0.055
Bodily pain	72.0 (23.6)	72.0 (23.2)	72.0 (26.6)	0.985
General health	66.7 (19.7)	66.7 (19.9)	66.8 (18.7)	0.126
Social functioning	91.4 (19.6)	91.6 (19.6)	90.2 (19.2)	0.604
Role-emotional	61.8 (21.5)	92.7 (24.1)	86.3 (31.5)	0.220
Vitality	92.0 (25.1)	61.9 (21.4)	61.1 (21.8)	0.560
General mental health	79.5 (16.6)	79.8 (16.4)	77.0 (18.4)	0.059
SF-36 summary scores, mean (SD)				
Physical component summary	45.7 (9.3)	45.8 (9.2)	45.70 (10.3)	0.277
Mental component summary	55.0 (8.1)	55.2 (8.0)	53.67 (9.1)	0.111

Note. Sf-36= 36-Item Short Form Health Survey. Higher scores on SF-36 subscales and components indicate better health related quality of life.

Table 2.

Association between cognitive domains and SF-36 subscale measures.

	Memory		Executive function		GF	
	β	t	β	t	β	t
Physical health subscales						
Physical functioning	0.04	1.35	0.05	2.10	−0.02	−0.89
Role-physical	0.05	1.90	0.06	2.16	−0.02	−0.62
Bodily pain	0.02	0.67	0.05	1.77	0.01	0.32
General health	0.05	1.95	0.12*	4.76*	0.03	1.35
Mental health subscales						
Social functioning	0.12*	4.76*	0.07*	2.96*	0.01	0.52
Role-emotional	0.07*	2.95*	0.10*	3.80*	0.02	0.81
Vitality	0.07*	2.83*	0.08*	3.30*	−0.02	−0.99
General mental health	0.12*	4.33*	0.11*	4.09*	0.10*	4.01*

Note.

*Indicates significant associations with p-value <0.005. All models are adjusted for age, gender (female as reference), race (white as reference), education, and medical comorbidity index. GF= general fluid ability. PCS= Physical component summary, MCS= Mental component summary

Table 3.

Association between cognitive domains and SF-36 summary scores.

	Memory		Executive function		GF	
	β	t	β	t	β	t
Physical component summary	0.02	0.54	0.05	2.00	−0.01	−0.44
Mental component summary	0.11*	4.1*	0.10*	3.94*	0.06	2.1

Note.

*Indicates significant associations with p-value <0.005. All models are adjusted for age, gender (female as reference), race (white as reference), education, and medical comorbidity index. GF= general fluid ability.

Table 4.

Hazard ratios for incident all-cause dementia and incident Alzheimer's dementia using baseline level of SF-36 subscale measures.

	Models for all-cause Dementia			Models for AD		
	HR	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
Physical health subscales						
Physical functioning	0.89	0.73–1.08	0.258	0.90	0.74–1.12	0.366
Role-physical	0.73	0.63–0.86	<0.001	0.76	0.64–0.90	0.002
Bodily pain	0.92	0.77–1.11	0.876	1.00	0.83–1.20	0.966
General health	0.84	0.72–1.06	0.166	0.86	0.70–1.08	0.174
Mental health subscales						
Social functioning	0.85	0.71–0.99	0.044	0.83	0.69–0.99	0.044
Role-emotional	0.80	0.71–0.90	<0.001	0.81	0.71–0.93	0.003
Vitality	0.86	0.70–1.06	0.146	0.94	0.74–1.18	0.580
General mental health	0.78	0.67–0.92	0.003	0.78	0.65–0.93	0.005

Note. Each unit change on HR represents one standard deviation change in the respective measure.

Table 5.

Hazard ratios for incident all-cause dementia and incident Alzheimer's dementia using baseline level of SF-36 summary score measures.

	Models for all-cause Dementia			Models for AD		
	HR	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
Physical component summary	0.87	0.72–1.06	0.160	0.88	0.72–1.10	0.273
Mental component summary	0.79	0.68–0.92	0.003	0.81	0.68–0.96	0.004

Note. Each unit change on HR represents one standard deviation change in the respective measure.