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Adherence to Medication Regimens is an Effective Indicator of Cognitive Dysfunction in Elderly Individuals

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Abstract

Background: Cognitive abilities strongly influence medication adherence among elderly individuals. We aimed to evaluate the relationship between medication adherence and cognitive decline using Lawton's instrumental activities of daily living (IADL) scoring system and the Mini-Mental State Examination (MMSE). **Methods:** Receiver–operating characteristic (ROC) curves were used to evaluate the IADL scores and MMSE results. **Results:** The ROC curve analysis of the IADL and MMSE results revealed that the *shopping* (MMSE cutoff = 22 points, sensitivity = 0.726, and specificity = 0.683) and *responsibility for own medications* (MMSE cutoff = 22 points, sensitivity = 0.759, and specificity = 0.720) categories were associated with declining IADL scores during early stage cognitive dysfunction. **Conclusion:** Declining IADL scores in the *shopping* and *responsibility for own medications* categories may be effective indices for predicting early-stage cognitive dysfunction in elderly individuals. Cognitive dysfunction screening at pharmacy counters may be useful.

Keywords

cognitive decline, medication adherence, instrumental activities of daily living (IADL), Mini-Mental State Examination (MMSE)

Introduction

Management of chronic comorbid conditions via medication requires strict adherence to treatment protocols and is often complicated by complex dosing schedules and the difficulties that are associated with properly administering the medications. Studies have demonstrated that elderly individuals' adherence to medication administration regimens is influenced more by the number of long-term medications used, the cost of the medications, the patient's satisfaction with care, and access to transportation, compared to age alone.[1,2] In addition, several studies have suggested that cognitive abilities significantly influence adherence to medication regimens[3-8] and that adherence requires a variety of complex cognitive skills, including the ability to access medication,[9] understanding prescriptions, and proper scheduling and administration of medication during daily activities.

The Lawton's instrumental activities of daily living (IADLs) scale determines an individual's ability to perform basic self-care tasks and the complex skills that are needed for successful independent living. The study has demonstrated that IADL may be an important indicator of elderly cognitive impairment,[10] and several other studies have demonstrated that the assessment of IADL is useful for detecting early dementia.[11-14] Thus, we hypothesize that an elderly individual's ability to effectively manage medication is not maintained, even in the absence of problems with daily care and before changes in activities of daily living (ADL) occur. Therefore, it is necessary to determine whether patients are unintentionally using drugs or altering their drug dosage and to simplify administration methods to facilitate effective management.

The purpose of this study was to evaluate the relationship between medication management abilities and cognitive decline in elderly study participants, using the IADL scoring system and the Mini-Mental State Examination (MMSE).

Methods

Study Design

This study was a retrospective cross-sectional study that was conducted between October 2010 and December 2013 at the

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National Center for Geriatrics and Gerontology (NCGG) hospital in Obu, Japan. This 320-bed hospital provides general care services and admits approximately 5000 patients per year (>50% of the patients are ≥75 years old). This study was approved by the ethics committee at the NCGG hospital.

Participants

The participants in this study were 3351 Japanese patients (1188 men and 2163 women) with a mean age of 78.9 years (standard deviation [SD] = 6.3 years, range = 65-103 years), who had received medical care for dementia at the NCGG hospital. The participants were administered a comprehensive cognitive function test, and their medication use was confirmed by clinical pharmacists. Medication adherence was family assessment, using the IADL category *responsibility for own medications*. The responses for this category consisted of *Is responsible for taking medication in correct dosages at correct time* (which indicates high medication adherence), *Takes responsibility if medication is prepared in advance in separate dosages,* and *Is not capable of dispensing own medication.*[15] The clinical characteristics of the study participants were retrieved from the hospital's medical records.

Measures

The ADL evaluation instruments that were used for this study included Lawton's IADL scale[15] and the Barthel Index score.[16] The IADL scale assesses 8 categories regarding self-care functional skills, including the *ability to use a telephone*, *shopping*, *food preparation*, *housekeeping*, *laundry*, *transportation use*, *responsibility for own medications*, and *ability to handle finances*.[15] The Barthel Index score assesses 10 self-care categories, including *feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfers, mobility,* and *stairs.*[16] The MMSE evaluates an individual's *orientation in time and space*, *attention*, *memory, language*, and *constructive skills*.[17] Comorbidity was assessed using the Charlson comorbidity index.[18] All data regarding the study participants' prescriptions were collected by pharmacists through a pharmacy database. Anticholinergic risk scale (ARS) scores were evaluated to determine the anticholinergic drugs' effects on cognitive function.[19]

Statistical Analysis

Normally distributed variables were expressed as mean ± SD. Receiver–operating characteristic (ROC) curves were used to calculate the areas under the curve (AUCs), 95% confidence intervals (CIs), standard errors (SEs), and cutoff points. Multivariate logistic regression analysis was used to identify the risk factors for nonadherence to medication regimens. The predictive ability of the final model was quantified using the Hosmer–Lemeshow statistical test for goodness of fit. A 2-sided *P* value of <.05 was considered statistically significant. SPSS software (version 22.0, SPSS Inc, Chicago, Illinois) was used for all statistical analyses.

Table 1. Study Participant Characteristics.

Variable	N = 3351
Age, years	78.9 ± 6.3
Sex, men/women	1188/2163
Education, years	10.1 ± 3.0
Barthel index score	90.3 ± 17.2
Charlson comorbidity index	1.2 ± 1.5
Mini-Mental State Examination score	19.7 ± 6.1
Disease, n (%)	
Dementia	
Alzheimer's-type dementia	1,704 (50.9)
Vascular dementia	75 (2.2)
Frontotemporal dementia	43 (1.3)
Lewy body dementia	154 (4.6)
Mixed dementia	253 (7.5)
Mild cognitive impairment	478 (14.3)
Normal-pressure hydrocephalus	46 (1.4)
Medication	
No. of medications	3.7 ± 3.1
Anticholinergic medication, n (%)	160 (4.8)
Alzheimer's disease medication, n (%)	1,298 (38.7)
Polypharmacy (≥5 medications), n (%)	916 (27.3)

Results

The characteristics of the 3351 study participants (1188 men and 2163 women) are shown in Table 1. The mean age of the study participants was 78.9 ± 6.3 years (range = 65-103 years), and their mean education duration was 10.1 ± 3.0 years. The mean Barthel index, Charlson comorbidity index, and MMSE scores were 90.3 ± 17.2, 1.2 ± 1.5, and 19.7 ± 6.1, respectively. Among the 3351 study participants, 2753 exhibited a variety of etiologies for their cognitive dysfunction, including Alzheimer's-type dementia (1704 participants, 50.9%), vascular dementia (75 participants, 2.2%), frontotemporal dementia (43 participants, 1.3%), Lewy body dementia (154 participants, 4.6%), mixed dementia (253 participants, 7.5%), mild cognitive impairment (478 participants, 14.3%), and normal pressure hydrocephalus (46 participants, 1.4%). The mean number of medications used was 3.7 ± 3.1, and the prevalence of participants with polypharmacy (≥5 medications) was 27.3%. Anticholinergic medication was used by 160 participants (4.8%), and Alzheimer's disease medication was used by 1298 participants (38.7%).

The analyses of the IADL scale scores and MMSE scores using the ROC curves are shown in Table 2. Male participants were evaluated using 5 of the 8 categories included in the IADL scale, and their mean IADL score was 3.0 ± 1.6. The MMSE cutoff points for the *ability of telephone use* and *shopping* among men were 18 points (AUC = 0.826, 95% CI = 0.791-0.862) and 22 points (AUC = 0.784, 95% CI = 0.757-0.810), respectively. The MMSE cutoff points for *mode of transportation* and *responsibility for own medications* among men were 21 points (AUC = 0.747, 95% CI = 0.719-0.776) and 22 points (AUC = 0.803, 95% CI = 0.778-0.828), respectively. The MMSE cutoff point for *ability to handle finances* among men was 20 points (AUC = 0.812, 95% CI = 0.782-0.842).

Table 2. Analysis of the Instrumental Activities of Daily Living Scale and Mini-Mental State Examination Using Receiver Operating Characteristic Curves.

State variable	AUC	95% CI	SE	Cutoff	Sensitivity	Specificity
Men						
A. Ability to use telephone	0.826	0.791-0.862	0.018	18	0.793	0.718
B. Shopping	0.784	0.757-0.810	0.013	22	0.726	0.683
C. Food preparation	–	–	–	–	–	–
D. Housekeeping	–	–	–	–	–	–
E. Laundry	–	–	–	–	–	–
F. Mode of transportation	0.747	0.719-0.776	0.014	21	0.674	0.674
G. Responsibility for own medications	0.803	0.778-0.828	0.013	22	0.759	0.720
H. Ability to handle finances	0.812	0.782-0.842	0.015	20	0.703	0.745
Women						
A. Ability to use telephone	0.815	0.788-0.842	0.014	17	0.756	0.732
B. Shopping	0.790	0.771-0.809	0.010	21	0.727	0.711
C. Food preparation	0.795	0.777-0.814	0.010	20	0.713	0.726
D. Housekeeping	0.783	0.754-0.813	0.015	18	0.692	0.738
E. Laundry	0.780	0.755-0.804	0.013	18	0.724	0.703
F. Mode of transportation	0.719	0.697-0.740	0.011	19	0.660	0.657
G. Responsibility for own medications	0.812	0.793-0.830	0.009	21	0.750	0.725
H. Ability to handle finances	0.826	0.805-0.847	0.011	18	0.738	0.754

Abbreviations: AUC, area under the curve; CI, confidence interval; SE, standard error.

Table 3. Risk Factors for Nonadherence to Medication Regimens.

	Univariate Analysis			Multivariate Analysis		
Variable	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
Polypharmacy, ≥5 medications	0.973	0.828-1.143	.738			
Anticholinergic risk scale score	1.185	1.046-1.343	.002	1.138	1.015-1.351	.030
Use of Alzheimer's disease medication	2.847	2.411-3.362	<.001	3.000	2.498-3.603	<.001
Sex, male	1.101	0.941-1.287	.230			
Age, ≥75 years	2.437	2.052-2.894	<.001	1.766	1.456-2.141	<.001
Barthel index score, <100	5.550	4.659-6.611	<.001	6.097	5.031-7.389	<.001

Abbreviations: Nagelkerke $R^2 = 0.292$; Hosmer–Lemeshow test, $P = 0.877$. CI, confidence interval.

Female participants were evaluated using all 8 categories in the IADL scoring system, and their mean IADL score was 5.0 ± 2.4. The MMSE cutoff points for *ability to use telephone* and *shopping* among women were 17 points (AUC = 0.815, 95% CI = 0.788-0.842) and 21 points (AUC = 0.790, 95% CI = 0.771-0.809), respectively. The MMSE cutoff points for *food preparation* and *housekeeping* were 20 points (AUC = 0.795, 95% CI = 0.777-0.814) and 18 points (AUC = 0.783, 95% CI = 0.754-0.813), respectively. The MMSE cutoff points for *laundry* and *mode of transportation* among women were 18 points (AUC = 0.780, 95% CI = 0.755-0.804) and 19 points (AUC = 0.719, 95% CI = 0.697-0.740), respectively. The MMSE cutoff points for *responsibility for own medications* and *ability to handle finances* among women were 21 points (AUC = 0.812, 95% CI = 0.793-0.830) and 18 points (AUC = 0.826, 95% CI = 0.805-0.847), respectively. Our results indicate that elderly men and women in the early stage of cognitive dysfunction are unable to perform the activities that are required for the *shopping* and *responsibility for own medications* categories.

Next, we investigated the risk factors for nonadherence to medication regimens using univariate analysis (Table 3). The following risk factors were found to be associated with nonadherence to medication regimens: polypharmacy, ARS score, use of Alzheimer's disease medication, sex, age (≥75 years), and Barthel index score (<100). As shown in Table 3, the following 4 factors exhibited significant differences after univariate analysis: ARS score ($P = .002$, odds ratio [OR]: 1.185, 95% CI: 1.046-1.343), use of Alzheimer's disease medication ($P < .001$, OR: 2.847, 95% CI: 2.411–3.362), ≥75 years old ($P < .001$, OR: 2.437, 95% CI 2.052-2.894), and Barthel index score <100 ($P < .001$, OR: 5.550, 95% CI: 4.659-6.611). Multivariate analysis with multiple logical regression of the following risk factors revealed an association with nonadherence: ARS score ($P = .030$, OR: 1.138, 95% CI: 1.015-1.351), use of Alzheimer's disease medication ($P < .001$, OR: 3.000, 95% CI: 2.498-3.603), age

($P < .001$, OR: 1.766, 95% CI: 1.456-2.141), and Barthel index score ($P < .001$, OR: 6.097, 95% CI: 5.031-7.389).

Discussion

This study revealed that elderly men and women in the early stage of cognitive failure are unable to perform the ADLs in the IADL categories of *shopping* and *responsibility for own medications*. In addition, our data revealed that advanced age, the ARS score, and the Barthel index score were predictors of nonadherence to medication regimens among participants with cognitive decline.

Several studies have discussed the relationship between IADL and MMSE scores and dementia,[20,21] and McGrory et al have demonstrated that the *shopping* and *ability to use telephone* categories in the IADL scale were sensitive for identifying and observing changes in functional abilities due to dementia.[20] Similarly, our results demonstrate that the MMSE cutoff points for the *ability to use telephone* predict the most progressed stage of cognitive dysfunction among men and women predict. Furthermore, De Lepeleire et al have reported that the use of the IADL score might change the general practitioner's diagnostic judgment for dementia.[21] Therefore, our findings are in agreement with those of De Lepeleire et al, although our study focused on medication adherence. In addition, several studies have suggested that patients who are receiving polypharmacy are prone to poor medication adherence, which is associated with increased mortality.[22-24] However, polypharmacy was not an indicator for poor medication adherence in our study. We hypothesize that this discrepancy may be related to elderly patients' lower number of physician-prescribed medications, due to clinicians' awareness of poor medication adherence in this population. The results from our study reveal a significant association between poor medication adherence and various factors, such as ARS score, use of Alzheimer's disease medication, advanced age, and low Barthel index scores. Furthermore, almost all participants who used Alzheimer's disease medication were diagnosed with dementia and exhibited reduced adherence to their medication regimens. In a previous study, Lowry et al reported that high ARS scores and low Barthel index scores were strongly associated with in-hospital mortality.[25] Furthermore, other studies have demonstrated that MMSE scores of <25 were associated with poor medication adherence,[5,26] while we found that the early stage of cognitive failure (MMSE score of <22) is unable to perform the ADLs in the IADL categories of *shopping* and *responsibility for own medications*. However, nonadherence in our study was determined via family-assessment IADL scores, and we suspect that differences in the assessment methods (health care workers vs family assessment) were responsible for this discrepancy.

A few limitations of our study should be considered. First, this study used a retrospective observational design, which cannot capture changes in cognitive decline over time. Second, medication adherence was based on family assessment and was not accurately determined by a clinical pharmacist. Unfortunately, the overall complexity of medication regimens is a major concern for patients with chronic conditions[27,28] and is associated with poor medication adherence.[29] Moreover, poor drug adherence is not an effective measure among patients with severe cognitive decline, as their family or caregiver often manages these patients' medications. Therefore, future research should focus on investigating the association between medication regimen complexity and poor medication adherence among elderly individuals who administer their own medication.

Conclusion

This study revealed that decreased IADL scores, especially for *shopping* and *responsibility for own medications*, may be effective indices for predicting early-stage cognitive dysfunction in elderly individuals. Furthermore, patients who use anticholinergic agents have poor ADL abilities, and their advanced age may increase the risk of poor medication adherence. These results indicate the potential utility of maintaining a screening system at pharmacy counters to detect cognitive dysfunction in elderly individuals.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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