Factors Associated with Self-reported Medication Adherence in Japanese Community-dwelling Elderly Individuals: The Nakajima Study

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Medication non-adherence in the elderly population is a major problem, preventing them from obtaining optimal therapeutic effects. Identifying the factors affecting medication adherence is crucial for improving and maintaining health among the elderly population and enhancing healthcare economy. The purpose of this study was to examine the prevalence of self-reported medication adherence, and identify the associated factors and the influence of health-related quality of life (HRQOL) in the Japanese community-dwelling elderly population. This cross-sectional study was part of the Nakajima study and targeted inhabitants aged ≥ 60 years who underwent health examinations in 2017. Data regarding medication adherence were acquired through interviews and self-administered questionnaires. Medication adherence was assessed using a visual analog scale, and HRQOL was assessed by EuroQol five-dimensional questionnaire with 3 levels. Among the 455 participants, low and high medication adherence were seen in 9.7% and 66.2% of the participants, respectively (visual analog scores < 80% and ≥ 95%, respectively). Medication adherence was significantly lower in participants taking medications ≥ 3 times daily than in those taking medications once or twice daily; a regimen involving drug administration ≥ 3 times daily had significantly lower odds of medication adherence. The use of a drug profile book and HRQOL had significant positive association with medication adherence. Our results suggest that lower dosing frequency and using a drug profile book was positively associated with medication adherence among elderly persons, which in turn could enhance their QOL.

Key words—drug profile book; medication adherence; QOL; pharmacist; older

INTRODUCTION

A rapidly aging population is a major concern in many countries, including Japan, and the demand for medication therapy for elderly persons is increasing.1) Elderly individuals are predisposed to poor medication adherence because of factors such as polypharmacy, multiple comorbidities, physical inability, and cognitive decline.2) Medication non-adherence among them contributes to a higher readmission rate, longer hospital stays, and a range of adverse outcomes resulting from reduced therapeutic responses.3,4) As such, non-adherence results in escalating avoidable healthcare costs. Moreover, several studies have reported that medication adherence affected health-related quality of life (HRQOL) of patients with certain diseases.5,6) Therefore, identifying the factors that affect medication adherence among the elderly population and designing effective intervention methods are crucial for improving and maintaining health status, and improving healthcare economy and QOL in the elderly population.

Multiple factors affect elderly individuals’ adherence to medications, and several reasons for non-adherence have been reported in earlier studies.7,8) Previous reports have suggested that factors affecting medication adherence in older adults include age, gender, education, depression, and cognitive functions. Additionally, multiple medications, dosing regimens, and types of medications have also been...
identified as influential factors. Poor communication with physicians and lack of follow-ups are also associated with patients’ medication adherence. However, most studies on medication adherence have focused on a specific disease and medication; they have not evaluated the overall medication adherence in the general elderly population. In addition, they were conducted among specific participants, as in monocentric studies.

This study aimed to evaluate self-reported medication adherence, and identify factors associated with medication adherence and impact on HRQOL in the Japanese community-dwelling elderly population.

MATERIALS AND METHODS

Study Setting and Participants The Nakajima study was a population-based longitudinal cohort study that investigated the cognitive decline of the elderly Japanese residents in Nakajima, Nanao City, Ishikawa Prefecture, Japan. The design of the Nakajima study has been described previously.9,10

The present cross-sectional study was conducted as a part of the Nakajima study that was supported by Nanao City. The criterion for inclusion of participants was age 60 years or older. As of April 1, 2016, a total of 2826 people aged 60 years or older were legally residing in Nakajima. Residence information listings were used to identify eligible participants and to send invitations for health examinations. Among the residents who underwent a health examination between January and December 2017, those who took one or more medications and answered the questionnaire about medication adherence were included in this study.

Participant Characteristics and Prescribing Information Data were collected from the mass health examinations conducted at town halls. Participants were required to complete self-administered questionnaires which included socio-demographic information (such as age and gender), medical history (such as hypertension, hyperlipidemia, and diabetes mellitus), and lifestyle habits in addition to assessing their neuropsychological functions. Cognitive functions were investigated using the Mini-Mental State Examination, with scores of ≤ 23 indicating cognitive impairment.11 HRQOL was evaluated using the EuroQol five-dimensional questionnaire with 3 levels (EQ5D-3L), which includes five dimensions (mobility, self-care, usual activities, pain, and anxiety/depression).12 In addition, we collected information concerning prescription medicines from drug profile books and drug information sheets, and measured the number of medication and dosing frequency. A drug profile book is a personal health record, and a Japan-specific medical method for recording personal medication history. It serves as a communication tool between patients, pharmacists, doctors, and other healthcare professionals. Stickers that provide details about prescriptions dispensed by pharmacies are affixed to the drug profile book. Medication adherence and information that is not included in drug profile book and drug information sheet (one-dose package and using of drug profile book) was acquired through face-to-face interviews with pharmacists.

Ethics Approval This study was approved by the Medical Ethics Review Board of Kanazawa University (approval number: 2186) and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent before enrolment.

Assessment of Medication Adherence For this study, we used a self-reported visual analog scale (VAS) to evaluate medication adherence. The VAS score was determined by measuring the distance (mm) on a 10-cm line between zero and the participant’s mark, providing a range of scores from 0 (no prescribed doses taken) to 100 (all doses taken).13 Adherence was categorized according to the VAS as follows: high adherence (≥ 95%), moderate adherence (80 to < 95%), and low adherence (< 80%). Additionally, the “adherence group” included participants with high adherence, and the “non-adherence group” included participants with moderate or low adherence.

Statistical Analysis Data are presented as numbers and percentages for categorical variables and as median [interquartile range] for numerical variables. Categorical variables were compared using the chi-square test, and numerical variables were compared using the Mann-Whitney U test. Multiple comparisons were performed using the Kruskal-Wallis and Steel-Dwass tests. We used the Kolmogorov-Smirnov test to check for normality of distribution. To identify factors that were independently associated with medication adherence, variables with a p value of less than 0.1 in the univariate analysis were introduced into a multivariate model using binary logistic regression with the forced entry method. Additionally, to
clarify the effect of medication adherence on HRQOL, we conducted a multiple linear regression analysis (stepwise selection) and the variables included in the model were the factors of participants’ characteristics, number of medications, which was a reported relevant variable to HRQOL in previous studies\(^{14,15}\), and VAS score. Associations are expressed as adjusted odds ratios (AORs) with 95% confidence intervals (CIs). A \( p \) value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS, Version 24.0 (IBM Corp., Armonk) and Esumi Excel Statistics, Version 7.0 (Esumi Corp., Tokyo).

### RESULTS

#### Participant Characteristics and Prescribing Information

Of the 645 potentially eligible participants aged \( \geq 60 \) years, 140 were excluded as they did not consume any medication. We further excluded 50 participants from the analysis for not responding to questionnaire items concerning medication adherence. Ultimately, the data obtained from 455 participants were analyzed.

The characteristics and prescription information of the participants are summarized in Table 1. The median age of the participants was 71 years (mean ± S.D.: 72.9 ± 7.5 years), of which nearly half...
Perfect 100. High adherence to medication was observed in 301 (93.5\%) groups prescribed 1–10 drugs per day, and 55.6\% (66.2\%) of the participants were men, and 59 (13.0\%) resided alone. The median number of medications used daily was 4 (mean \pm S.D.: 5.1 \pm 3.8), and the median daily dosing frequency was 2 (mean \pm S.D.: 2.2 \pm 1.2).

Assessment of Medication Adherence
The overall VAS score of the participants was 99 [90, 101] (minimum: 29, maximum: 100, mean \pm S.D.: 93.5 \pm 10.9), with 216 participants (47.5\%) scoring a perfect 100. High adherence to medication was observed in 301 (66.2\%) participants, moderate adherence in 110 (24.2\%), and low adherence in 44 (9.7\%).

Number of Medications and Medication Adherence
The association between medication adherence and the number of medications is shown in Fig. 1. There were no significant differences between the groups (p = 0.150). However, participants who were prescribed 11 or more drugs per day (95 [19, 100]) tended to have a lower VAS score than those who were prescribed 1–5 (100 [29, 100]) and 6–10 drugs (98 [53, 100]) per day. The rate of use of one-dose package was 14.2\% in 1–5 drugs, 51.4\% in 6–10 drugs, and 55.6\% in \geq 11 drugs (p < 0.001).

Dosing Frequency and Medication Adherence
The association between medication adherence and dosing frequency is shown in Fig. 2. There were significant differences observed between the groups (p = 0.014). The group with a dosing frequency of \geq 3 times per day (97 [29, 100]) showed a significantly lower VAS score than the groups with a dosing frequency of once (100 [50, 100], p = 0.038) and twice (99 [50, 100], p = 0.026) per day. However, no significant difference was observed between the groups with dosing frequencies of once and twice per day (p = 0.999).

Factors Associated with Medication Adherence
Table 2 shows the characteristics and prescription information associated with medication adherence in the univariate analysis. A dosing frequency of \geq 3 times daily, use of 11 or more prescribed drugs, use of antidiabetic drugs, and use of inhalation drugs were associated with significant differences between the adherence and non-adherence groups (p = 0.011, 0.021, 0.014 and 0.011, respectively). Furthermore, factors with a p value between 0.05 and 0.1 included consultation with multiple clinical departments, use of a drug profile book, and use of antilipidemic drugs.

A logistic regression analysis was performed using factors with p values < 0.1 in the univariate analysis as covariates. The results showed that the use of a drug profile book (AOR: 2.174, 95\% CI: 1.326–3.562, p = 0.002) and a dosing frequency of \geq 3 times per day (AOR: 0.617, 95\% CI: 0.381–0.998, p = 0.049) were independent factors associated with medication adherence among elderly participants (Table 3).

Impact of Medication Adherence on HRQOL
The overall HRQOL score of the participants was 0.848 [0.739, 1.000]; 1.000 [0.796, 1.000] in the adherence group, and 0.796 [0.727, 1.000] in the non-adherence group. The regression coefficients in the multiple linear regression analysis, which was conducted to evaluate the effect on HRQOL, are documented in Table 4.
medications, and VAS score was retained as explanatory variables for HRQOL. However, the effect of medication VAS score on HRQOL was weak ($\beta = 0.092$, $p = 0.034$).

**DISCUSSION**

Medication non-adherence in the elderly population is a major problem that must be addressed so that they can obtain optimal therapeutic effects from their medications. In this study, we investigated self-reported medication adherence and identified the associated factors with adherence in the elderly population.

There are a variety of ways to measure medication adherence such as using self-reports, pill counts, electronic monitoring systems, and prescription refill rates.\(^{(16)}\) We used VAS, which is an easy and quick self-reported scale to evaluate medication adherence. In our study, the median VAS score was 99\%, which was high and similar to the results of previous studies which used VAS to evaluate medication adherence among Japanese elderly.\(^{(17)}\) However, there is a possibility that these results may be overestimated because of the variation between subjective and objective evaluations.\(^{(18},(19)}\)

The cut-off point for medication adherence using VAS was 80–100\% in previous studies\(^{(17},(20)-(25)}\) and is generally 80\%; however, this threshold is not always appropriate as it has been arbitrarily defined\(^{(26)}\) and varies for different diseases.\(^{(27},(28)}\) Meanwhile, the median VAS score in previous studies were 91–100\%\(^{(17},(20)-(25),29-32)}\) because of overestimation of self-reported data.\(^{(18},(19)}\) Moreover, a good association between VAS $\geq 95$\% and HbA1c was reported in dia-

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**Table 2. Factors Associated with Medication Adherence in the Univariate Analysis**

| Characteristics                                      | Variables | Non-adherence $n = 154$ | Adherence $n = 301$ | $p$ value |
|------------------------------------------------------|-----------|-------------------------|---------------------|-----------|
| Age                                                  | 71 [66, 79] | 71 [67, 79]             | 0.351               |
| Gender, male                                         | 74 (48.1) | 139 (46.2)              | 0.705               |
| Employed                                             | 57 (37.3) | 105 (35.2)              | 0.672               |
| Education, $> 9$ years                                | 83 (53.9) | 160 (53.2)              | 0.881               |
| Single-living                                        | 19 (12.3) | 40 (13.4)               | 0.746               |
| Smoking                                              | 13 (8.4)  | 26 (8.6)                | 0.944               |
| Drinking alcohol                                     | 61 (39.6) | 128 (42.7)              | 0.532               |
| MMSE                                                  | 28 [26, 29] | 28 [25, 29]            | 0.738               |
| Prescribing information                              |           |                        |                     |
| Multiple hospital/clinic use                         | 42 (27.3) | 66 (21.9)               | 0.205               |
| Multiple clinical departments consultation            | 52 (35.1) | 76 (26.4)               | 0.058               |
| Multiple pharmacy use                                 | 23 (15.8) | 30 (10.4)               | 0.109               |
| Use of drug profile book                             | 108 (70.1) | 235 (78.3)             | 0.054               |
| Daily use of medication $\geq 11$                     | 23 (14.9) | 24 (8.0)                | 0.021*              |
| Daily dosing frequency $\geq 3$ times                 | 62 (40.8) | 85 (28.8)               | 0.011*              |
| Medication category                                  |           |                        |                     |
| Antihypertensive                                     | 102 (67.5) | 203 (68.8)             | 0.786               |
| Antilipidemic                                        | 72 (47.4) | 112 (38.4)             | 0.067               |
| Antidiabetic                                         | 44 (28.8) | 56 (18.6)               | 0.014*              |
| Dosage form                                          |           |                        |                     |
| Oral                                                 | 153 (99.4) | 293 (97.3)             | 0.145               |
| Patch                                                | 25 (16.2) | 46 (15.3)               | 0.791               |
| Embrocation                                           | 13 (8.4)  | 26 (8.6)                | 0.944               |
| Inhalation                                           | 7 (4.5)   | 4 (1.3)                 | 0.011*              |
| Eye drop                                             | 15 (9.7)  | 27 (9.0)                | 0.788               |
| Suppository                                          | 1 (0.6)   | 1 (0.3)                 | 0.628               |
| Injection                                            | 3 (1.9)   | 12 (4.0)                | 0.249               |
| One-dose package                                     | 32 (29.1) | 54 (23.2)               | 0.238               |

* $p < 0.05$. Categorical variables are shown as numbers (percentages), and numerical variables are shown as median (inter-quartile range). MMSE: Mini-Mental State Examination.
Table 3. Binary Logistic Regression Models for Factors Associated with Medication Adherence

| Predictor variables                  | AOR  | 95% CI       | p value |
|--------------------------------------|------|--------------|---------|
| Clinical department consultation     | Single Reference | 0.816 | 0.503–1.323 | 0.409 |
|                                      | Multiple Reference | 2.174 | 1.326–3.562 | 0.002* |
| Use of drug profile book             | No Reference | 0.764 | 0.363–1.605 | 0.477 |
|                                      | Yes Reference | 0.617 | 0.381–0.998 | 0.049* |
| Number of medications taken daily    | 1–10 Reference | 0.764 | 0.363–1.605 | 0.477 |
|                                      | ≥ 11 Reference | 0.617 | 0.381–0.998 | 0.049* |
| Dosing frequency per day             | 1–2 Reference | 0.764 | 0.363–1.605 | 0.477 |
|                                      | ≥ 3 Reference | 0.617 | 0.381–0.998 | 0.049* |
| Use of antilipidemic drugs           | No Reference | 0.703 | 0.458–1.080 | 0.108 |
|                                      | Yes Reference | 0.619 | 0.375–1.022 | 0.061 |
| Use of antidiabetic drugs            | No Reference | 0.305 | 0.084–1.103 | 0.070 |
|                                      | Yes Reference | 0.305 | 0.084–1.103 | 0.070 |

Total n = 416 (only responses without missing values in any of the included variables are included in the regression model). *p < 0.05. AOR: adjusted odds ratio. CI: confidence interval.

Table 4. Multiple Linear Regression Analysis That Evaluated the Association with Health-related Quality of Life

| Variables                        | B (S.E.) | β     | p value* |
|----------------------------------|----------|-------|----------|
| Age                              | -0.006 (0.001) | -0.233 | <0.001 |
| Gender, male                     | 0.057 (0.015) | 0.158 | <0.001 |
| Number of medications            | -0.012 (0.002) | -0.257 | <0.001 |
| Medication compliance rate       | 0.002 (0.001) | 0.092 | 0.034 |

*p < 0.05 was considered as statistically significant. S.E.: standard error.

Diabetes mellitus patients.33 Therefore, we followed strict criteria for VAS scores in our study: moderate or low adherence (<95%) was defined as the non-adherence group, and high adherence (≥95%) was defined as the adherence group.

The relationship between the number of medications being taken and medication adherence in elderly persons has been reported in many previous studies.3,34,35 In the present study, no significant relationship was observed between the number of medications being taken and medication adherence; although there was a trend showing that participants taking 11 or more medications daily had lower adherence than those taking 10 or fewer. We believe that the effect of number of medications on medication adherence was masked because of the use of one-dose packages by participants who consumed large number of medications, which improved medication adherence.36 Therefore, our results support the notion that a reduction of polypharmacy in elderly persons should be pursued to improve medication adherence.

Existing research focusing on specific diseases has confirmed an inverse relationship between dosing frequency and medication adherence.37,38 In this study, medication adherence was lower when the participants were taking medication ≥3 times daily than when they were taking medication once or twice daily (p = 0.038 and 0.026, respectively). Furthermore, a daily regimen including ≥3 medications was linked with a significant decrease in adherence (AOR: 0.617, 95% CI: 0.381–0.998, p = 0.049). These results suggest that a dosing frequency of ≤2 doses per day may improve medication adherence among the elderly population. In our study, there were no significant difference in medication adherence for dosing frequencies of once or twice per day. Although, once-daily regimens have been recommended in previous studies to improve medication adherence.38,39 Therefore, the optimal dosing frequency to improve medication adherence in the elderly population remains unidentified.

The guidelines for proper use of medications for elderly persons, which was issued by the Japanese Ministry of Health, Labour and Welfare, proposed the unified management of prescription information by utilizing a drug profile book for the improvement of medication adherence.40 However, there has been no previous evidence demonstrating its effectiveness. In the present study, we found that the use of a drug profile book was relevant in predicting high medication adherence. It has been reported that patient-
pharmacist communication resulting from the use of drug profile books has led to improvements in patients’ medication awareness and behavior.\textsuperscript{41} In addition, previous research has suggested that medication adherence improves when pharmacists sufficiently explain medications through counseling.\textsuperscript{42} Therefore, intervention by pharmacists, such as using drug profile books, could have a positive effect on medication adherence in elderly participants. However, this effect needs to be verified in future studies.

The factor associated with HRQOL in this study was age, gender, number of medications and the medication adherence. Some of these results were in line with previous studies which were evaluated using EQ5D-3L\textsuperscript{43,44}: women reported lower HRQOL than men; and HRQOL declined with age. In addition, several studies had shown similar results to ours that increasing the number of medications was related with lowering HRQOL.\textsuperscript{14,15} In contrast, the association between adherence and HRQOL in the studies targeting specific diseases such as hypertension, diabetes mellitus and epilepsy has been reported.\textsuperscript{5,60} Our study, consisting of community-dwelling elderly participants, showed a similar association. Therefore, our results suggest that improvement of medication adherence may improve the HRQOL irrespective of the diseases.

Our study has several limitations. First, the results of this study do not precisely apply to medication adherence, because we only investigated VAS score which was the rate of medication compliance. The psychosocial aspects of medication adherence require further evaluation. Second, the participants voluntarily participated in a mass health examination; therefore, there might have been a selection bias that led to the inclusion of a high proportion of health-conscious participants, resulting in over estimation of medication adherence. However, the study targeted general community-dwelling elderly persons; hence, we were able to avoid biases that arise from being limited to specific diseases and medical facilities. Third, the medication adherence might also be over-estimated as they were self-reported.\textsuperscript{18,19} Finally, our study had a cross-sectional design, which precludes causal inferences. Therefore, it is possible that the full scope of the influences of the factors affecting medication adherence were not captured. These findings should be further examined in longitudinal studies.

In conclusion, medication adherence is a vital point of concern not only for the healthcare system but also for a better healthcare economy. Our study showed that the prevalence of self-reported medication adherence was high in Japanese community-dwelling older adults. The results of this study indicate that low dosing frequency and using a drug profile book was positively associated with medication adherence of elderly persons. Therefore, pharmacists should make effective use of drug profile books for communication with patients. Furthermore, our results also indicate a significant association between medication adherence and QOL in elderly.

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\textbf{Author Contributions} Natsuko Ishida conceived and designed the study and wrote the draft of the manuscript. Yurina Tokumoto, Yukio Suga, and Junko Ishizaki contributed to the analysis and interpretation of data and assisted in the preparation of the manuscript. All other authors contributed to data collection and interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript. The project director of the Nakajima study was Masahito Yamada.

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