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Validation of the 5-Item Medication Adherence Report Scale in Older Stroke Patients in Iran

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Abstract

Background: There is a lack of feasible and validated measure to self-assess medication adherence for older patients with stroke. In addition, the potential determinants on the medication adherence for older patients with stroke remain unclear.

Objective: (1) examining the psychometric properties of a five-item questionnaire on medication adherence (Medication Adherence Report Scale; MARS-5); (2) exploring the determinants of medication adherence.

Methods: Patients with stroke aged over 65 years (N=523) completed the MARS-5 and the Hospital Anxiety and Depression Scale. Moreover, the medication possession rate (MPR) was calculated to measure the objective medication adherence. Several clinical characteristics (stroke types, blood pressure, comorbidity, HbA1c, number of prescribed drugs, fasting blood glucose, and total cholesterol) and background information were collected. We used Rasch analysis with differential item functioning (DIF) test to examine the psychometric properties.

Results: All the five items in the MARS-5 fit in the same construct (i.e., medication adherence), no DIF items were displayed in the MARS-5 across gender, and the MARS-5 total score was highly correlated with the MPR ($r=0.7$). Multiple regression models showed that MARS-5 and MPR shared several similar determinants. In addition, the variance of the MARS-5 ($R^2=0.567$) was explained more than that of the MPR ($R^2=0.300$).

Conclusions: The MARS-5 is a feasible and valid self-assessed medication adherence for older patients with stroke. Moreover, several determinants were found to be related to the medication adherence for older patients with stroke. Healthcare providers may want to take care of these determinants to improve medication adherence for such population.

Keywords: adherence; elderly; questionnaire; stroke

Introduction

Stroke is the leading cause of death: it is the fifth, second, and sixth leading cause of death in the US,¹ Europe,² and Iran,³ respectively. In addition, stroke often results in functional disability and substantially impact on an individual's well-being.^{4,5} After the first stroke, the cumulative risk of stroke recurrence is 11.1% after 1 year and 26.4% after 5 years.⁶ Previous researchers identified one cause of recurrence is the medication nonadherence as some studies have shown positive relationships between lower medication adherence and greater incidence of stroke symptoms.^{7,8} Also, guidelines for secondary prevention after stroke have explicitly recommended using appropriate medications to control or reduce both blood pressure and cholesterol level.^{9,10} Hence, promoting the medication adherence among stroke patients is critical, and investigating the potential determinants for medication adherence among patients suffering from stroke is important.

Some studies have highlighted the importance of medication adherence in patients with stroke and investigated potential determinants. The determinants include beliefs toward medications,^{11,12} low density lipoprotein cholesterol (LDL-C),¹³ knowledge on medications,¹⁴ and emotion.¹⁵ That is, more positive beliefs toward medications, lower LDL-C, more knowledge on medications, and less emotional distress are positively correlated with better medication adherence. Although information of the aforementioned determinants can be of help in daily clinical practice, some knowledge gaps exist regarding whether these determinants are applicable for older patients with stroke in clinical practice.

To the best of our knowledge, no studies have investigated the aforementioned issue in an older population with stroke. Given the different characteristics (e.g., healthy literacy and taking polypharmacy treatment or not) between older and younger patients with stroke, the determinants of the medication adherence might be somewhat different between the two types of patients with stroke. For example, as compared with younger patients, older patients

may have poorer health literacy (such as the understanding to the importance and handling adverse effects of each medication), a greater need for polypharmacy treatment (older patients are more likely than younger patients to have more comorbidities, and need to take more types of medications), and more often need to take multiple doses each day.¹⁶ As a review study has concluded a variety of potential factors related to medication adherence,¹⁷ empirical studies are needed to conduct a comprehensive assessment of the determinants for medication adherence including demographics, clinical characteristics and emotional distress. For example, age and educational level were weakly associated with adherence for older people.¹⁸

Another practical and important issue is to have a feasible and valid instrument to measure medication adherence for patients with stroke. A potential candidate to assess medication adherence is Medication Adherence Report Scale (MARS), which has a 10-item version (MARS-10) and a five-item version (MARS-5). The MARS-10 has been validated for its unidimensionality among people with mental illness;^{19,20} however, no studies have examined the psychometric properties of MARS-10 in people with stroke. Similarly, we found that the psychometric evaluation of the MARS-5 has only been done on populations other than those with stroke using classical test theory.²¹⁻²³ Although some studies have argued whether the MARS-5 can accurately measure the drug adherence,^{24,25} other studies have found that the MARS-5 can accurately measure the medication adherence.^{26,27} In fact, Lin et al.²⁸ has concluded that the different characteristics among various diseases may contribute to different findings in the accuracy of the MARS-5. It thus highlights importance to conduct psychometric assessment of the MARS-5 in the specific disease population of interest.

We proposed to validate the MARS-5 for feasibility of use to measure medication adherence in older patients with stroke. The main reason is that the MARS-5 is shorter than

the MARS-10; therefore, MARS-5 will have less administration burden than MARS-10 do. In addition, although the psychometric properties of the MARS-5 have yet been verified in people with stroke, some studies have used the MARS-5 to assess the medication adherence in patients with stroke.^{11,12} Specifically, we will adopt modern test theory (e.g., Rasch model) to analyze the psychometric properties of the MARS-5 to fill in the literature gap.

The major benefits of using Rasch to test psychometric properties include (1) it separately estimates the person ability and item difficulty; therefore, the psychometric results are not sample-dependent; (2) it produces an ordinal-to-interval conversion table based on the probability that a person responds to a certain answer of an item; a special unit (i.e., *logit*) is thus generated and has the additive characteristics; (3) it helps to identify which item is an unfair item across subgroups. That is, differential item functioning (DIF) in the Rasch can help us to know whether subgroups interpret any item in different considerations.²⁹ As males and females are very likely to have different thoughts based on the different brain structures,³⁰ testing DIF for MARS-5 across gender is of great interests to the healthcare providers. Specifically, we should identify whether the score difference of the MARS-5 reflects the true differences between genders or is due to various interpretations toward the MARS-5.³¹ Hence, we claimed that testing DIF across gender for the MARS-5 is a prerequisite before clinical application.

The purposes of this study were (1) to examine the psychometric properties of the MARS-5 in a sample consisting of elderly patients with stroke; (2) to explore the determinants of medication adherence in an older sample with stroke.

Methods

Sampling and setting

The study participants were patients with stroke who had been discharged from five hospitals in Tehran and Qazvin in 2016. Inclusion criteria were: (1) patients with stroke

confirmed by neuroimaging; (2) aged 65 years or above; (3) being responsible to take their own medication without any help; (4) having the ability to read and write Persian, including the ability of providing informed consent to participate in the study. Exclusion criteria were: (1) patients with moderate-to-severe cognitive impairment (i.e., mini-mental state examination score < 18); (2) patients with dysphasia, aphasia, liver failure, or renal dysfunction. Ethics approval was obtained from the review committees of different universities and all participants were provided with written informed consents.

Measures

Clinical characteristics. Type of stroke and comorbidity were collected from patient's medical records. However, two research assistances measured blood pressures and drew blood for hemoglobin A1c and lipids in this study. Standard protocol was used to measure systolic and diastolic blood pressure (SBP and DBP) using calibrated mercury sphygmomanometers and appropriate size cuff. The level of HbA1c, which indicates average level of blood glucose levels over 3 months, was obtained from blood samples and was assessed using the high-pressure liquid chromatography (HPLC) method. Fasting blood glucose was also assessed using enzymatic method. Serum lipid (i.e., total cholesterol, TC) was directly measured using an esterase oxidase method. Patients' comorbidity was measured using the Charlson comorbidity index.

Emotional distress. Hospital Anxiety and Depression Scale (HADS) was used to collect the information of emotional distress, including anxiety and depression performance. The HADS contains 14 items; seven items measure anxiety and another seven items measure depression using four response categories, and a higher score indicates higher levels of anxiety or depression.³² The validity of the HADS has been established in patients with stroke.³³ Also, the Persian version of the HADS for Iranian use had satisfactory psychometric properties, including linguistic validity, internal consistency, known-group validity, construct validity,

and unidimensionality for each subscale.^{34,35} In the current study, the internal consistency was acceptable for the HADS: $\alpha=0.83$ for anxiety subscale and $\alpha=0.89$ for depression subscale.

Medication adherence. The MARS-5 and MPR were used to observe the medication adherence of the participants. The MARS-5, a self-reported instrument, contains five items regarding the performance on medication adherence. Each item was rated on a five-point Likert scale, and the range of the MARS-5 total score is between 5 and 25. A higher score of the MARS-5 represents a better medication adherence.^{11,36} In addition, the Persian version of the MARS-5 for Iranian use had satisfactory internal consistency.³⁷ In the current study, the internal consistency was acceptable for MARS-5 ($\alpha=0.85$).

The MPR was presented using the number of days on dispensed medications divided by the number of total days. Specifically, the days on dispensed medications were defined by the number of days on which medications were dispensed to the participants during the study period. The total days were defined by the total number of days in the study period. The calculated values were then multiplied by 100, and presented in percentage. All related information was collected monthly from 13 pharmacies among the five hospitals in Tehran and Qazvin and included the total number of pills prescribed along with the dates of each prescription. We assessed the cardiovascular medication, blood pressure-lowering and diabetes medication adjusted for inpatient days and medication refills prior to enrollment date as well as information registered at two months' post discharge on change in prescriptions.

Procedure

Patients with stroke were screened at hospitals by three trained physicians in terms of the eligibility. After confirming the eligibility, each participant was asked to sign the informed consent, and then complete the study measures including MARS-5 and HADS at two months after discharge. The MPR was also calculated two months after discharge. Clinical measures were then collected at two months after discharge (i.e. two months

post-discharge) to assess the predictive validity of the MARS.

Data analysis

Two statistical programs were used for data analysis: DIF and Rasch models using WINSTEPS 3.75.0, and all other analyses using SPSS 23.0 (IBM Corp., Armonk, NY.).

Rasch analysis was conducted using rating scale model to test the item fit of the MARS-5 and the unidimensionality of the entire MARS-5. The item fit was assessed using two mean square (MnSq): the information-weighted fit statistic (infit) and the outlier-sensitive fit statistic (outfit), which ranges between 0.5 and 1.5 suggest well fit.^{38,39} The unidimensionality was assessed using principal component analysis on the Rasch-retrieved standardized residuals, and first component's eigenvalue < 2 indicates unidimensionality.²⁹ Person separation reliability reported by the Rasch analysis should be less than 0.7 to indicate adequate consistency among the MARS-5.⁴⁰ The Likert-type scale of the MARS-5 was examined for its categorical functioning: the successive responses for each item score are located in their expected orders. Specifically, average difficulty of the scores and score thresholds (the thresholds between every two scores) should both should monotonically increase with scores.⁴¹ DIF analysis was conducted to investigate whether male and female patients with stroke interpret the MARS-5 differently. A substantial DIF item indicates that the item description has different difficulties for different subgroups (different genders in this study) of respondents.⁴² We adopted the usual method to identify DIF items: a DIF contrasts (i.e., the difference of difficulty between two groups) > 0.5 suggests a substantial DIF.⁴³

We examined the relationship between MARS-5 and the MPR using the Pearson correlation coefficient. Afterward, we constructed two regression models to explore the factors for medication adherence measured by using the MARS-5 and MPR, respectively. We used a total score of MARS-5 and MPR as two dependent variables; demographic variables

(age, gender, marital status, monthly family income, and educational level), clinical characteristics (comorbidity, fasting blood glucose test, blood pressure, total cholesterol, and HbA1c), and emotional distress (anxiety and depression) as the independent variables. All the continuous variables (age, fasting blood glucose test, blood pressure, total cholesterol, HbA1c, and emotional distress) could be viewed as normal distributed. The multicollinearity among the independent variables was acceptable.

Our final sample (N=523) was sufficient for all our analyses. The required sample size for Rasch to achieve a stable estimate is 250,⁴⁴ especially for the questionnaire using 5-point Likert type scale such as MARS-5. In terms of regression analyses, Austin and Steyerberg⁴⁵ suggested each variable needs 15 to 25 participants. Given that we used 13 variables in each regression model, the sample size fell between 195 and 325.

Results

Table 1 presents the demographic information, clinical characteristics, emotional distress performance, and medication adherence for the participants (N=523).

(Insert Tables 1 here)

The Rasch analysis showed that the MARS-5 had satisfactory item properties: infit MnSq = 0.74 to 1.25; outfit MnSq = 0.68 to 1.40. The first eigenvalue of the principal component analysis on the standardized residuals was 1.6, which suggests unidimensionality of the MARS-5. The person separation reliability (0.74) of the MARS-5 was adequate. The categorical functioning of the rating scale in the MARS-5 was in the anticipation of monotonic increment: the average difficulties were -6.16 for score 1; -0.28 for score 2; 2.92 for score 3; 4.92 for score 4; and 6.57 for score 5. Also, the score thresholds were monotonically increased: -9.01 for score 1 to 2; -0.01 for score 2 to 3; 3.76 for score 3 to 4; and 5.27 for score 4 to 5. No substantial DIF items were displayed across genders as all the absolute DIF contrasts were less than 0.5 (Table 2).

(Insert Table 2 here)

The correlation between the MARS-5 total score and the MPR was strong ($r=0.70$, $p<0.001$). In the model with MARS-5 as dependent variable, gender, marital status, monthly family income, and all the clinical characteristics were significant predictors. In the MPR model, gender, monthly family income, and clinical characteristics except comorbidity and HbA1c were significant predictors. Anxiety was significantly associated with MARS-5 but not with MPR, while depression was significantly associated with MPR but not with MARS-5. In addition, female gender, fair to good monthly family income (i.e., $>500\$$), and number of prescribed drugs were associated with higher MARS-5 and/or MPR score. Unmarried status, having comorbidities, higher levels of fasting blood glucose, blood pressure, total cholesterol, HbA1c, anxiety and depression were associated with lower MARS-5 and/or MPR score (Table 3). As the model using MARS-5 as dependent variable had more significant predictors than the model using MPR as dependent variable, the former model ($R^2=0.567$) explained more variance than did the later ($R^2=0.300$).

(Insert Table 3 here)

Discussion

Our psychometric findings first demonstrate that the MARS-5 is a valid measure to assess the medication adherence in older patients with stroke. Based on the satisfactory results in Rasch analysis, and a high correlation with MPR ($r=0.7$), the MARS-5 may be a useful tool for clinicians and researchers capture medication adherence. We extended the knowledge about psychometric properties of MARS-5 from classic test theory finding to the Rasch analysis, including DIF across gender. That is, all the MARS-5 items are invariant across gender: male and female patients interpret the five items similarly without substantial DIF, and the items have the same meanings for both genders.

The unidimensionality of the MARS-5 is in agreement with another study on children

and their caregivers.²¹ Although no studies have used Rasch analysis on the MARS-5, our results are comparable to the findings of two recent studies which applied Rasch analysis to the ten-item MARS in people with mental illness.^{19,20} All of their and our findings in fit statistics were satisfactory: infit MnSq ranged between 0.74 and 1.25 in our study; between 0.90 and 1.03 in Fond et al.¹⁹; and between 0.92 and 1.03 in Zemmour et al.²⁰

Furthermore, it has been a debate whether the MARS-5 is an appropriate measure for medication adherence²⁴⁻²⁷ and different characteristics of disease patients may affect the accuracy of the MARS-5.²⁸ Based on our rigorous psychometric findings (unidimensionality of the MARS-5, no DIF items in the MARS-5, and a high correlation with MPR), we are confident that the MARS-5 is able to accurately measure the medication adherence for older patients with stroke. Nonetheless, future studies are warranted to corroborate with our findings because this is the first study to investigate the psychometric properties of the MARS-5 on patients with stroke.

Another important issue in psychometric properties for the MARS-5 is the DIF across gender. Different subgroups are highly likely to interpret the item contents in different meanings, especially for the subgroups that usually have different perspectives, such as the gender subgroups we tested in the study. In order to fairly assess the item scores across subgroups, DIF should be tested before combining or comparing the subgroups scores.⁴² Because of no DIF items were displayed, combined using MARS-5 scores from male and female older patients with stroke or comparing MARS-5 scores between male and female older patients with stroke are acceptable.

Based on the sound psychometric properties, we further investigated the possible determinants for medication adherence in older patients with stroke. The associations between demographic variables and medication adherence in our regression model were similar to the findings of two review studies: female, living with a spouse, and high monthly

family income are correlated with increased compliance; age and educational level are weakly associated with adherence, especially for older people.^{17,18} Also, similar to the findings of Phillips et al.,¹⁵ our regression model demonstrated that emotional distress was negatively correlated to good medication adherence.

In terms of clinical characteristics, we found that when the patients had higher scores on Charlson comorbidity index, their medication adherence was poorer. The findings of clinical characteristics are somewhat similar to Cummings et al.'s study⁷ in which blood pressure was positively correlated with medication adherence in hypertension patients. In addition, our other clinical characteristics indicated that poor medication adherence existed in patients with stroke who had more risk in diabetes mellitus. Because diabetes mellitus is highly correlated with stroke⁴⁶ and patients with stroke are highly likely to have recurrence of stroke,⁶ clinicians may want to pay additional attention to these significant clinical characteristics for patients with stroke. Moreover, our findings also correspond to the guidelines suggesting controlling blood pressure and cholesterol level.^{9,10}

There are some limitations in the study. First, only less than 10% of our participants were diagnosed as intracerebral hemorrhage, and our results may not be able to generalize to patients with this type of stroke. Second, the study only recruited patients from five hospitals in Tehran and Qazvin; thus, the generalizability of our study results might not be applicable to the entire Iran. Third, because our sample was Iranian without moderate to severe cognitive impairment, our results were unable to generalize to the patients with stroke in other countries or those with cognitive impairment. Fourth, our results might be influenced by the different stroke types in our study. Specifically, the pathophysiologic mechanisms between transient ischemic stroke, ischemic stroke, and hemorrhagic stroke are quite different. The different mechanisms might affect the medication adherence of the patients with stroke in different levels. Therefore, future studies using homogeneous sample in stroke type (e.g.,

transient ischemic stroke) and diversity in other populations (e.g., Westerns and Asians) are warranted to corroborate our findings. Moreover, future research should consider measuring functional status of the patients.

Conclusions

The MARS-5 has satisfactory psychometric properties according to the Rasch model. The results indicate that the scale is unidimensional, the response scale (i.e., the five-point Likert-type scale) functions appropriately, the targeting is acceptable and no DIF items were displayed across gender. Thus, the MARS-5 might be a useful measure for both clinicians and researchers to assess medical adherence.

What's New?

- Medication Adherence Report Scale (MARS-5) is a feasible self-reported questionnaire to assess medication adherence for Iranian elders with stroke.
- MARS-5 shows robust psychometric properties, especially its unidimensionality, in the Iranian elders with stroke.

Table 1 Participant characteristics (N=523)

	Mean±SD or n (%)
Demographic information	
Age (Year)	72.9±6.5
Gender (Male)	220 (42.1)
Marital status (living with a spouse)	417 (79.7)
Educational level	
No formal/primary school	108 (20.7)
Primary school	170 (32.5)
Secondary school or higher	245 (46.8)
Monthly family income	
Poor (0-500\$)	189 (36.1)
Fair (500-1000\$)	310 (59.3)
Good (>1000\$)	24 (4.6)
Clinical characteristics	
Diagnosis	
Ischemic stroke	377 (72.1)
Transient ischemic stroke	108 (20.7)
Intracerebral hemorrhage	38 (7.3)
Comorbidity (Yes)	256 (48.9)
Fasting blood glucose test (mg/dL)	142.92±67.49
HbA1c	7.23±1.32
Systolic blood pressure (mmHg)	127.26±14.98
Diastolic blood pressure (mmHg)	77.46±9.31
Total cholesterol (mg/dL)	180.53±78.09

Number of prescribed drugs	3.4±1.8
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Emotional distress^a

Anxiety	11.2±4.1
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Depression	10.1±4.4
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Medication adherence

Five item Medication Adherence Report Scale	21.6±3.3
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(MARS-5)

Medication possession rate (MPR)	61.6±19.1
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^aMeasured using Hospital Anxiety and Depression Scale

Table 2. Rasch analysis on the five item Medication Adherence Report Scale (MARS-5; N=523)

Item#: <i>content</i>	Difficulty	Infit MnSq	Outfit MnSq	Difficulty for males	Difficulty for females	DIF contrast
Item 1: <i>change dosage</i>	0.00	0.95	0.87	0.07	-0.05	0.12
Item 2: <i>forget to take</i>	1.78	1.25	1.40	2.02	1.59	0.43
Item 3: <i>stop taking</i>	-1.18	1.12	1.06	-1.15	-1.22	0.07
Item 4: <i>skip one of dosages</i>	0.05	0.87	0.83	-0.22	0.24	-0.46
Item 5: <i>take less than prescribed</i>	-0.65	0.74	0.68	-0.81	-0.54	-0.27

DIF=differential item functioning.

DIF contrast=difficulty for males minus difficulty for females (positive values implies more difficult for males and negative values implies more difficult for females).

Acceptable Infit and Outfit MnSq is between 0.5 and 1.5; acceptable DIF contrast is < 0.5.

Table 3. Multiple linear Regression models on five item Medication Adherence Report Scale (MARS-5) and medication possession rate (MPR) (N=523)

	MARS-5				MPR			
	Coefficient	Standard Error	Standardized Coefficient	p-value	Coefficient	Standard Error	Standardized Coefficient	p-value
Demographics								
Age (year)	-0.02	0.02	-0.04	0.23	-0.18	0.12	-0.06	0.16
Female gender (Ref: male)	0.59	0.22	0.09	0.01	3.39	1.60	0.09	0.03
Secondary school or higher (Ref: ≤primary)	-0.14	0.30	-0.02	0.64	1.22	2.23	0.03	0.58
Currently unmarried (Ref: married)	-0.88	0.34	-0.11	0.01	-3.80	2.49	-0.08	0.13
Fair and good socioeconomic	0.68	0.24	0.10	0.01	4.55	1.78	0.11	0.01

mic status

(Ref: poor)

Clinical

characteristics

stics

Number of prescribed drugs	0.43	0.08	0.22	<0.0 01	2.05	0.57	0.19	<0.0 01
Comorbidity	-0.60	0.25	-0.09	0.02	-1.12	1.84	-0.03	0.55
Fasting blood glucose test (mg/dL)	-0.02	0.00	-0.48	<0.0 01	-0.10	0.01	-0.35	<0.0 01
Mean arterial pressure (mmHg)	-0.08	0.01	-0.24	<0.0 01	-0.40	0.08	-0.22	<0.0 01
Total cholesterol (mg/dL)	-0.01	0.00	-0.16	<0.0 01	-0.02	0.01	-0.10	0.02
HbA1c	-0.35	0.10	-0.14	<0.0 01	-0.68	0.72	-0.05	0.34

Emotional

distress

Anxiety ^a	-0.12	0.04	-0.15	0.003	0.15	0.29	0.03	0.60
Depression	-0.04	0.04	-0.05	0.30	-0.66	0.28	-0.15	0.02

a

Model**statistics**

F-value	46.40	(<0.001)	15.07	(<0.001)
(p-value)				
Degrees of freedom	13,		13,	
	460		460	
R ²	0.567	(0.555)	0.300	(0.280)
(Adjusted R ²)				

^aMeasured using Hospital Anxiety and Depression Scale.

Significant coefficients are in **bold**.

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