Validity of Korean Versions of the Multiple Sclerosis Impact Scale and the Multiple Sclerosis International Quality of Life Questionnaire

So-Young Huh, a Jungnam Joo, b Su-Hyun Kim, c Ae-Ran Joung, c Kibyung Park, b Woojun Kim, d Min Su Park, e Ho Jin Kim c

aDepartment of Neurology, Kosin University College of Medicine, Busan, Korea
bBiometric Research Branch, Research Institute and Hospital of National Cancer Center, Goyang, Korea
cDepartment of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea
dDepartment of Neurology, The Catholic University of Korea College of Medicine, Seoul, Korea
eDepartment of Neurology, College of Medicine, Yeungnam University College of Medicine, Daegu, Korea

Background and Purpose Assessment of the health-related quality of life (HRQoL) is important in clinical evaluations of multiple sclerosis (MS) patients for quantifying the impact of illness and treatment on their daily lives. Although MS-specific HRQoL instruments have been used internationally, there are no data regarding HRQoL instruments specifically designed for patients with MS in Korea. The objective of this study was to determine the reliability and validity of the Korean Multiple Sclerosis Impact Scale (MSIS-29) and the Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire.

Methods Fifty-six patients with MS were recruited from June 2009 to February 2010 at the National Cancer Center in Korea. The original English versions of the MSIS-29 scale and the MusiQoL questionnaire were translated into Korean and evaluated for their acceptability, reliability, and validity.

Results The patients were aged 36.5 ± 8.6 years (mean ± SD; range, 20–56 years). Their score on the Expanded Disability Status Scale was 2.0 ± 1.9 (mean; range, 0–7.5), and their disease duration was 5.2 ± 4.7 years (mean ± SD; range, 1–24 years). The Korean versions of the MSIS-29 and MusiQoL questionnaires showed satisfactory psychometric properties, including construct validity (item-internal consistencies of 0.59–0.95 and 0.59–0.92, respectively; item-discriminant validities of 95–100% and 93.8–100%), internal consistency (Cronbach’s alpha coefficients of 0.96–0.97 and 0.77–0.96), reliability (intraclass correlation coefficients of 0.78–0.90 and 0.50–0.93), unidimensionality (Loevinger scalability coefficients of 0.70–0.78 and 0.63–0.90), and acceptability. External validity testing indicated the presence of significant correlations between similar aspects of the two questionnaires.

Conclusions The Korean translated versions of the MSIS-29 and MusiQoL questionnaires demonstrated reliability and validity for measuring HRQoL in Korean patients with MS.

Key Words multiple sclerosis, health-related quality of life, MSIS-29, MusiQoL.

Introduction

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system that causes neurologic disability in young adults. Patients with MS face not only physical disabil-
ity but also neuropsychiatric problems such as anxiety and depression due to unpredictable relapse.\textsuperscript{1,2} MS has a significant negative impact on the health-related quality of life (HRQoL),\textsuperscript{3} which is an individual patient’s comprehensive perception about multiple aspects of life that include his or her physical, psychological, and social circumstances. Measuring HRQoL is expected to be important for patients with MS because the results can be used to improve the detection of unrecognized aspects of disease, assist clinicians with establishing treatment goals, and facilitate communication between physicians and patients.\textsuperscript{4} Moreover, measuring HRQoL is regarded as a standard part of new MS trials because traditional measurements such as the Expanded Disability Status Scale (EDSS), magnetic resonance imaging, and relapse rate cannot accurately assess the quality of life.\textsuperscript{5} Various HRQoL instruments for assessing patients with MS have been developed and validated,\textsuperscript{6,7} but there is currently no validated HRQoL instrument designed specifically for Korean patients with MS. Therefore, to provide a comprehensive assessment for Korean patients with MS, a validated Korean version of an HRQoL questionnaire is needed.

This study selected the Multiple Sclerosis Impact Scale (MSIS-29) and the Multiple Sclerosis International Quality of Life (MusiQoL) questionnaires as two MS-specific instruments,\textsuperscript{8,9} since general HRQoL evaluations are less sensitive to a specific disease such as MS. MSIS-29 and MusiQoL questionnaires have been used for both clinical trials and epidemiological studies, and they provide self-administered, multidimensional, and patient-based HRQoL assessments. The purpose of this study was to translate the MSIS-29 and MusiQoL questionnaires into Korean, and then to adapt and validate their use for Korean patients with MS.

**Methods**

**Korean translation**

The MSIS-29 and MusiQoL questionnaires were translated from the original English versions into Korean by two bilingual translators. Physicians reviewed the initially produced Korean versions, which were then back-translated into English by a bilingual physician. Both English versions were compared for consistency in order to detect the presence of ambiguous or inadequate items, and then they were used to produce the final Korean versions.

**Participants**

Patients with MS were recruited between June 2009 and February 2010 at the National Cancer Center in Korea. The patients were diagnosed with MS according to McDonald criteria at least 6 months before recruitment. The patients indicated that they were willing to complete the self-administered questionnaires. We excluded patients who were suffering from a severe relapse or unstable medical conditions, patients with an EDSS score greater than 8, and patients with apparent cognitive dysfunction or other systemic chronic illness. The study was approved by the Institutional Review Board of the National Cancer Center (approval no. NCCCTS-11-409) and was performed in accordance with the Declaration of Helsinki.

**Survey questionnaire details**

The MSIS-29 contains 29 items on 2 subscales: physical impact (PHY, 20 items) and psychological impact (PSY, 9 items). The MusiQoL questionnaire contains 31 items that measure perceived health in the following 9 dimensions: activities of daily living (ADL, 8 items), psychological well-being (PWB, 4 items), symptoms (SYM, 4 items), relationships with friends (RFr, 3 items), relationships with family (RFa, 3 items), sentimental and sexual life (SSL, 2 items), rejection (REJ, 2 items), coping (COP, 2 items), and relationships with the healthcare system (RHS, 3 items). The global MusiQoL score (referred to henceforth as “MusiQoL Index”) was obtained by averaging the scores for the various MusiQoL dimensions. Each item in both evaluations was scored on a 5-point scale, with 1 representing ‘never/not at all’, 2 representing ‘rarely/a little’, 3 representing ‘sometimes/somewhat’, 4 representing ‘often/a lot’, and 5 representing ‘always/very much’. The scores were reversed for a negatively worded item, and hence higher scores indicated a lower HRQoL. Scores on each dimension or item were transformed into a scale from 0 to 100. Protest or retest items were substituted for the missing items if one or two items were missing.

**Validation study design**

Original validation studies were used as references in this study.\textsuperscript{10,11} Patients were evaluated at the study entry (V1) and 21±7 days later (mean±SD; V2) via self-completion of the MSIS-29 and MusiQoL questionnaires. An experienced neurologist also evaluated patients based on sociodemographic data; type of MS; EDSS score;\textsuperscript{12} Fatigue Severity Scale (FSS-9) score, where fatigue was considered to be present if the total score is 36 or more;\textsuperscript{13} and the Korean version of the Patient Health Questionnaire (PHQ-9) for quantifying depression, where depression was considered to be present when the total PHQ-9 score is 10 or more.\textsuperscript{14,15}

This study included assessments of the internal validity, internal consistency reliability, reproducibility, discriminant validity, external validity, and acceptability, as described below. All data analyses were performed using R statistical software (version 2.12.1).
Internal validity
The item-internal consistency (IIC) and item-discriminant validity (IDV) were used to identify the construct validity. IIC was determined by estimating the correlation among items with the same dimension. An IIC value of at least 0.4 is recommended as indicating adequate consistency. The IDV was assessed as the correlation between items in the same dimension and items in different dimensions.

Floor and ceiling effects
A floor or ceiling effect was considered to be present if more than 15% of the respondents achieved the lowest or highest possible score, respectively.

Internal consistency reliability
The internal consistency reliability was based on the degree of item redundancy, as measured by Cronbach’s alpha coefficients. The internal consistency was considered to be high if the coefficient exceeded 0.7 for group comparisons.

Reproducibility
Reproducibility was determined by the test-retest intraclass correlation coefficient (ICC) among patients who stated that there had been no disease evolution between the two tests (V1 and V2). ICC values of 0.6–0.8 and >0.8 were considered to be indicative of good and excellent reliabilities, respectively.

Unidimensionality
The presence of unidimensionality in a dimension indicated that all items of that dimension tended toward the same concept that was investigated, and was assessed using the Loevinger scalability coefficient (H). The unidimensionality was considered to be strong for H values between 0.5 and 1.0.

Discriminant validity
The discriminant validities of the MSIS-29 scale and MusiQoL questionnaires were determined by comparing dimension-scale scores across different patient groups that were expected to differ in terms of sociodemographic factors (age, gender, disease duration, employment status, marital status, financial independence, and education status) or clinical factors (EDSS and type of MS). Dimension-scale scores of qualitative variables were compared between different patient groups using one-way analysis of variance (ANOVA). Spearman’s correlation coefficients were used for quantitative variables such as age and EDSS. Additionally, the group-difference construct validity between the EDSS score and each dimension of the evaluation instruments was examined by one-way ANOVA with post-hoc comparison using relative efficiency (RE) values, where RE = subscale score/total scale score, and so RE >1 indicates that the subscale was better than the instrument’s total score for measuring group differences.

External validity
The external validity is the extent to which the results obtained using one instrument can be generalized to other instruments. To determine the external validity, relationships of each dimension were assessed using Spearman’s rank correlation coefficients among the MSIS-29, MusiQoL, PHQ-9, and FSS-9 evaluations. A high external validity was indicated by Spearman’s correlation coefficients.

Table 1. Multi-item internal construction validity, internal consistency, reproducibility, and unidimensionality of the MSIS-29 and MusiQoL questionnaires

| Dimension | No. of items | IIC (min–max) | IDV (min–max) | IDV (%) | Floor (%) | Ceiling (%) | Cronbach’s alpha | ICC | Loevinger H |
|-----------|--------------|---------------|---------------|---------|-----------|-------------|----------------|-----|-------------|
| MSIS-29   |              |               |               |         |           |             |                 |     |             |
| PHY       | 20           | 0.59–0.91     | 0.45–0.73     | 95      | 19.6      | 0           | 0.97            | 0.9 | 0.7         |
| PSY       | 9            | 0.72–0.95     | 0.51–0.68     | 100     | 10.7      | 5.4         | 0.96            | 0.78| 0.78        |
| MusiQoL   |              |               |               |         |           |             |                 |     |             |
| ADL       | 8            | 0.59–0.88     | -0.17–0.75    | 93.75   | 14.3      | 1.8         | 0.94            | 0.93| 0.74        |
| PWB       | 4            | 0.86–0.92     | -0.08–0.78    | 100     | 14.3      | 5.4         | 0.96            | 0.84| 0.9         |
| SYM       | 4            | 0.63–0.75     | -0.02–0.72    | 96.88   | 21.4      | 1.8         | 0.85            | 0.89| 0.63        |
| RFa       | 3            | 0.65–0.87     | -0.28–0.37    | 100     | 3.6       | 12.5        | 0.89            | 0.5 | 0.76        |
| RFe       | 3            | 0.60–0.88     | -0.16–0.39    | 100     | 25        | 3.6         | 0.88            | 0.6 | 0.75        |
| SSL       | 2            | 0.63          | -0.09–0.48    | 100     | 7.1       | 30.4        | 0.77            | 0.7 | 0.66        |
| REJ       | 2            | 0.89          | -0.22–0.72    | 100     | 17.9      | 12.5        | 0.94            | 0.61| 0.9         |
| COP       | 2            | 0.81          | -0.18–0.69    | 100     | 64.3      | 1.8         | 0.89            | 0.77| 0.85        |
| RHS       | 3            | 0.67–0.85     | -0.07–0.42    | 100     | 35.7      | 1.8         | 0.88            | 0.66| 0.75        |

ADL: activities of daily living, COP: coping, H: Loevinger scalability coefficient, ICC: intraclass correlation coefficient, IDV: item-discriminant validity, IIC: item-internal consistency, MSIS-29: Multiple Sclerosis Impact Scale, MusiQoL: Multiple Sclerosis International Quality of Life, PHY: physical impact, PSY: psychological impact, PWB: psychological well-being, REJ: rejection, RFa: relationships with family, RFr: relationships with friends, RHS: relationships with the healthcare system, SSL: sentimental and sexual life, SYM: symptoms.
| Type of MS (mean±SD)*     | MS-29 | MusiQoL |
|---------------------------|-------|---------|
| RRMS (n=36)               | 18.5±19.01 | 39.8±29.47 |
| PPMS (n=2)                | 56.25±19.45 | 51.39±21.61 |
| SPMS (n=2)                | 63.75±33.59 | 55.36±35.00 |
| MoMS (n=11)               | 4.89±10.24 | 2.38±29.49 |
| CIS (n=5)                 | 8.75±15.51 | 11.44±18.88 |

| Sex (mean±SD)*            |        |         |
|---------------------------|--------|---------|
| Male (n=24)               | 20.7±24.4 | 32.4±30.7 |
| Female (n=32)             | 15.9±19.3 | 37.5±29.9 |

| Education (mean±SD)*      |        |         |
|---------------------------|--------|---------|
| Below college (n=15)      | 23.8±28.2 | 46.3±36.1 |
| Above college (n=41)      | 15.8±18.5 | 31.3±27.0 |

| Marital status (mean±SD)* |        |         |
|---------------------------|--------|---------|
| Married (n=28)            | 18.8±23.1 | 33.7±29.2 |
| Single (n=28)             | 17.1±20.3 | 36.9±31.4 |

| Employment status (mean±SD)* |        |         |
|-------------------------------|--------|---------|
| Employed (n=25)              | 14.7±20.3 | 29.3±27.3 |
| Unemployed (n=31)            | 20.5±22.6 | 40.1±31.8 |

| Financial independence (mean±SD)* |        |         |
|-----------------------------------|--------|---------|
| INDEP (n=21)                      | 19.0±22.5 | 31.9±29.6 |
| DEP (n=35)                        | 17.3±21.3 | 37.4±30.6 |

| Religion status (mean±SD)*       |        |         |
|----------------------------------|--------|---------|
| Religious (n=25)                 | 13.3±17.6 | 28.4±23.2 |
| Non-religious (n=31)             | 21.7±24.0 | 40.9±34.0 |

Table 2. Effects of patient clinical characteristics on each dimension
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man’s rank correlation coefficient exceeding 0.5.23

Acceptability
The acceptability was estimated from the proportion of missing values and the evaluation completion rate.

Results
In total, 56 MS patients were recruited from the MS clinic of the National Cancer Center in Korea. The patients were aged 36.5 ± 8.6 years (range, 20–56 years), their disease duration was 5.7 ± 4.7 years (range, 1–24 years), and 32 of them (57.1%) were female. Twenty-eight of the patients (50.0%) were married, 25 (44.6%) were employed, 25 (44.6%) identified themselves as being religious, and 41 (73.2%) had higher than college education. The MS classification determined that 5 (8.9%) had clinically isolated syndrome suggestive of MS (CIS), 11 (19.6%) had McDonald MS, 36 (64.3%) had relapsing remitting MS (RRMS), 2 (3.6%) had primary progressive MS (PPMS), and 2 (3.6%) had secondary progressive MS (SPMS). Their EDSS score was 2.0 ± 1.9 (range, 0–7.5). Fifteen patients with MS (26.8%) had depression (total PHQ-9 score ≥ 10) and 24 (42.8%) had fatigue (total FFS-9 score ≥ 36).

Internal validity
The internal validity was confirmed by acceptable IIC and IDV values. The IIC correlations ranged from 0.59 – 0.95 for the MSIS-29 and 0.59 – 0.92 for the MusiQoL questionnaire. The IDV ranged from 95% to 100% for the MSIS-29 and from 93.8% to 100% for the MusiQoL questionnaire (Table 1).

Floor and ceiling effect
The floor effect was greater than 15% for MSIS-29 PHY and MusiQoL SYM, RFa, REJ, RHS, and especially COP. A notable ceiling effect was found for MusiQoL SSL (30.4%).

Internal consistency reliability
The internal consistency reliability was high for all dimensions, as verified by Cronbach’s alpha coefficients ranging from 0.96 to 0.97 for the MSIS-29 and from 0.77 to 0.96 for the MusiQoL questionnaire (Table 1).

Reproducibility
The reproducibility was excellent for the MSIS-29 (ICC=0.78–0.90) and good for the MusiQoL questionnaire (ICC=0.50–0.93) (Table 1).

Unidimensionality
The unidimensionality for each dimension was acceptable (H

Table 2. Continued

| MSIS-29 | MusiQoL | Index |
|---|---|---|
| PHY | PSY | ADL | PWB | SYM | RFa | RFr | SSL | REJ | COP | RHS | Index |
| Age | 0.282 | 0.156 | 0.195 | 0.024 | 0.071 | -0.093 | 0.171 | 0.137 | 0.000 | 0.035 | 0.209 | 0.207 | 0.244 |
| Disease | 0.242 | 0.220 | 0.149 | 0.057 | 0.220 | 0.195 | 0.071 | 0.313 | 0.209 | 0.195 | 0.109 | 0.174 | 0.071 |
| EDSS | 0.273 | 0.421 | 0.256 | 0.237 | 0.417 | 0.256 | 0.071 | 0.313 | 0.209 | 0.195 | 0.109 | 0.174 | 0.071 |
| | 0.67 | 0.45 | 0.43 | 0.42 | 0.45 | 0.43 | 0.07 | 0.17 | 0.17 | 0.07 | 0.17 | 0.17 | 0.07 |

One-way analysis of variance: Spearman’s correlation coefficient (r).

A detailed analysis of variance, Spearman’s correlation coefficient within each questionnaire, ADL: activities of daily living, CIS: clinically isolated syndrome suggestive of MS, COP: coping, DEP: financial dependence, EDSS: Expanded Disability Status Scale, FFS: fatigue, global index: MusiQoL Index, global index: MusiQoL, Index: global index, Index: global index, Index: global index.
range, 0.70–0.78 for the MSIS-29 and 0.63–0.90 for the MusiQoL questionnaire) (Table 1).

**Discriminant validity**

The discriminant validity measures are listed in Table 2. MSIS-29 PHY and MusiQoL ADL, REJ, COP, and Index differed between different types of MS. The scores for these dimensions were highest (worst HRQoL) for patients with SPMS or PPMS, followed by the patients with RRMS, and lowest for patients with McDonald MS and CIS.

MusiQoL PWB was significantly better in patients who identified themselves as being religious than in those who did not. Other sociodemographic characteristics including gender, age, disease duration, marital status, employment status, and financial independence did not significantly affect the MSIS-29 and MusiQoL dimension scores.

Multiple Sclerosis Impact Scale-29 PHY and MusiQoL ADL were strongly correlated with EDSS scores ($r=0.67$ and 0.63, respectively; $p<0.001$) (Table 2). We also estimated the correlation between each dimension and graded EDSS group, when the patients were divided into three categories, according to included disability severity in functional score with accounting the distribution of patient by EDSS scores: Group 1 ($n=37$), $0 \leq$ EDSS score $<2.5$; Group 2 ($n=12$), $3 \leq$ EDSS score $<4$; and Group 3 ($n=7$), EDSS score $\geq 4$. A linear trend test indicated that all dimensions of MSIS-29 and MusiQoL ADL, PWB, REJ, COP, and Index became worse as the EDSS grade increased (Table 3). MSIS-20 PHY, MusiQoL ADL, and MusiQoL Index were suitable for distinguishing between groups when the RE was used. MusiQoL ADL was better than MSIS-29 PHY for detecting EDSS group differences (RE=$2.64$ vs. 1.37) (Table 3).

Depression (PHQ-9) and fatigue (FSS-9) scales were significantly correlated with scores for all MSIS-29 dimensions ($r=0.72–0.86$ and 0.58–0.65, $p<0.001$) (Table 4). PHQ-9 scores were most strongly correlated with MusiQoL PWB, followed by MusiQoL Index, ADL, and SYM. When we analyzed group differences according to depression (PHQ-9 $\geq 10$ vs. $<10$) by independent-samples $t$-test, not only MusiQoL PWB, Index, ADL, and SYM, but also MusiQoL COP and REJ were significantly higher in patients who had depression (Table 4). The FSS-9 score was only correlated with MusiQoL Index and PWB in the qualitative analysis or group comparison study (Table 4).

**External validity**

The external validity between the MSIS-29 and MusiQoL scale is quantified in Table 5. The correlation was strongest between MSIS-29 PHY and MusiQoL ADL ($r=0.90$, $p<0.001$). In addition, MusiQoL PWB, SYM, and Index were correlated with MSIS-29 PHY ($0.71$, $0.65$, and 0.78, $p<0.001$). MSIS-29 PSY was also strongly correlated with MusiQoL PWB ($r=0.84$, $p<0.001$), followed by MusiQoL SYM, ADL, and Index ($r=0.82$, 0.79, and 0.87, $p<0.001$). However, none of the MSIS-29 dimensions reflected the social relationships (MusiQoL RFr, RFa, and RHS) or MusiQoL SLS.

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**Table 3.** Ascending EDSS-score comparisons by scale scores using post-hoc $t$-tests (Group 1: 0$\leq$EDSS$<2.5$; Group 2: 3$\leq$EDSS$<4$; Group 3: 4$\leq$EDSS)

| Dimension | Group 1, n=37 (mean±SD) | Group 2, n=12 (mean±SD) | Group 3, n=7 (mean±SD) | RE | Group 1 vs. Group 2 | Group 2 vs. Group 3 | Group 1 vs. Group 3 | Linear trend value |
|-----------|------------------------|------------------------|------------------------|----|-------------------|-------------------|-------------------|-------------------|
| MSIS-29   |                        |                        |                        |    |                   |                   |                   |                   |
| PHY       | 8.65±11.69             | 25.83±22.61            | 53.39±19.67            | 1.37| <0.001            | <0.001            | <0.001            | <0.001            |
| PSY       | 28.45±27.23            | 42.13±33.22            | 59.92±27.16            | 0.31| 0.466             | 0.030             | 0.588             | 0.01              |
| MusiQoL   |                        |                        |                        |    |                   |                   |                   |                   |
| ADL       | 15.03±15.67            | 34.38±27.15            | 69.64±20.23            | 2.64| 0.011             | <0.001            | 0.001             | <0.001            |
| PWB       | 25.51±27.61            | 42.19±32.87            | 54.46±22.74            | 0.54| 0.245             | 0.049             | 1.000             | 0.016             |
| SYM       | 20.61±23.66            | 30.21±21.62            | 33.04±28.12            | 0.13| 0.690             | 0.632             | 1.000             | 0.211             |
| RFr       | 55.18±29.49            | 57.64±11.49            | 44.05±24.4             | 0.11| 1.000             | 0.921             | 0.840             | 0.307             |
| RFa       | 37.61±29.17            | 37.5±26.71             | 33.33±28.46            | 0.01| 1.000             | 1.000             | 1.000             | 0.718             |
| SSL       | 62.16±32.61            | 76.04±22.27            | 69.64±36.7             | 0.15| 0.562             | 1.000             | 1.000             | 0.564             |
| REJ       | 32.43±27.4             | 45.83±34.27            | 60.71±41.1             | 0.22| 0.585             | 0.089             | 0.940             | 0.030             |
| COP       | 8.11±16.46             | 12.5±24.43             | 35.71±35.67            | 0.23| 1.000             | 0.008             | 0.077             | 0.003             |
| RHS       | 21.85±22.6             | 26.39±29.69            | 25.21±15.2             | 0.02| 1.000             | 1.000             | 1.000             | 0.75              |
| Index     | 27.55±15.44            | 38.64±14.91            | 49.88±12.86            | 1.00| 0.093             | 0.002             | 0.368             | <0.001            |

ADL: activities of daily living, COP: coping, EDSS: Expanded Disability Status Scale, MSIS-29: Multiple Sclerosis Impact Scale, MusiQoL: Multiple Sclerosis International Quality of Life, PHY: physical impact, PSY: psychological impact, PWB: psychological well-being, RE: relative efficiency (=subscale score/total scale score), REJ: rejection, RFa: relationships with family, RFr: relationships with friends, RHS: relationships with the healthcare system, SSL: sentimental and sexual life, SYM: symptoms.
Table 4. Spearman’s correlation coefficients and comparison of group differences between dimension scores of the HRQoL assessments (MSIS-29 and MusiQoL questionnaire), depression scale (PHQ-9), and fatigue scale (FSS-9).

| Variable | PHY | ADL | ADE | PST | PSY | COP | REJ | SSL | FSS-9* | PHQ-9* |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|--------|--------|
| Score ≥10 | 0.72 | 0.77 | 0.83 | 0.79 | 0.81 | 0.65 | 0.75 | 0.62 | 0.82 | 0.88 |<0.001 |
| Score <10 | 0.54 | 0.50 | 0.48 | 0.52 | 0.58 | 0.60 | 0.66 | 0.57 | 0.36 | 0.41 |<0.001 |

Discussion

The purpose of this study was to adapt and validate translated MSIS-29 and MusiQoL questionnaires for Korean patients with MS. The translated MSIS-29 and MusiQoL questionnaires exhibited good acceptance, as indicated by low rates of missing data and short completion times.

The internal consistency reliability ranged between 0.96 to 0.97 for the MSIS-29 and 0.77 to 0.96 for the MusiQoL scale. Additionally, the ICC values on all subscales for the test-retest reliability were satisfactory (0.78–0.90 for the MSIS-29 and 0.50–0.93 for the MusiQoL scale). Other studies have found ICC values between 0.65 to 0.82 for the MSIS-29 and 0.63 to 0.89 for the MusiQoL scale, which were similar to the values in the current study. These results indicate that the Korean versions of the MSIS-29 and MusiQoL questionnaires exhibit satisfactory reliability.

We correlated the scores on the MSIS-29 and MusiQoL questionnaire subscales with EDSS scores, disease duration, age, and sociodemographic factors in order to assess the construct validity. Although the mean EDSS score was lower than in other studies (2.0 vs. 3.2–5.0), the physical factors in the two Korean HRQoL instruments reflected those in the EDSS. Notably, the correlation between MSIS-29 PHY and the EDSS score was stronger in our study than in a Norwegian study (0.67 vs. 0.38). In accordance with the original MusiQoL study, an evaluation of differences in HRQoL according to types of MS showed that SPMS and PPMS patients had the worst HRQoL. However, a statistically significant correlation was not observed due to the small number of SPMS and PPMS patients.

In contrast, another study found that patients with SPMS have better HRQoL owing to increasing acceptance of the disease among patients with a longer disease duration. Therefore, the inclusion of a sufficient number of patients and taking the disease duration into account are necessary for elucidating the relationship between HRQoL and type of MS.

A correlation between HRQoL instruments and sociodemographic factors (e.g., education status and employment status) has been reported, whereas our study found no such correlation. This discrepancy could be due to certain characteristics of our study population, such as a mild degree of physical disability and a high level of education.
Depression and fatigue were associated with both the physical and mental components of the HRQoL instruments in our study. Depression strongly influences HRQoL in MS and is reportedly present in more than 50% of MS patients, which is approximately three times the prevalence in the general population. In our study, 27% of patients with MS had depression (scores of ≥10 on the PHQ-9 scale), which was about twice the percentage for a general Korean population included in a similar study involving the PHQ-9 (13.8%). Also, the PHQ-9 score was significantly associated with both mental dimensions (MSIS-29 PSY and MusiQoL PWB, REJ, and COP) and physical dimensions (MSIS-29 PHY and MusiQoL ADL). The patterns of correlations in the HRQoL evaluations were similar for the FSS-9 scale (i.e., fatigue) and the PHQ-9 scale (i.e., depression). This result may be attributable to the strong interactions that exist between depression and fatigue in MS.

Assessments of the external validity of the MSIS-29 with the MusiQoL questionnaire showed correlations between different dimensions; for example, MSIS-29 PHY was strongly correlated with MusiQoL PHY and PWB. Although these results might reflect interactions between physical and psychological factors, other studies have produced similar results. For example, a Polish survey found strong correlations between MSIS-29 PHY and MusiQoL ADL and PWB (r=0.804 and 0.523, p<0.001), and that MSIS-29 PSY was also correlated with MusiQoL ADL and PWB (r=0.589 and 0.713, p<0.001). Additionally, MSIS-29 PHY was correlated with the emotional-wellbeing scale in the Functional Assessment of Multiple Sclerosis instrument. Therefore, further research is needed to explore the robustness of the external validity between instruments because the external validation between the MSIS-29 and MusiQoL scale has not been categorically confirmed.

The design of the present study was subject to several limitations. First, our study was conducted on a small sample. Nevertheless, the pattern of the results obtained was quite comparable to that of the original versions. Second, there was a potential selection bias due to the EDSS scores of our studied population being lower and the inclusion of a higher percentage of patients with CIS or McDonald MS (28.9%) relative to other validation studies. As a result, the floor effects varied considerably between dimensions, and our data may have reflected a higher HRQoL than in other studies. Third, no comparable validated HRQoL evaluation is currently available for Korean MS patients that could be used for assessing the external validation. We were therefore only able to perform comparisons between our instruments. However, we were able to adequately address this problem by comparison with studies performed in other countries. Fourth, there was a notable ceiling effect (30.4%) for MusiQoL SSL. However, this is consistent with ceiling effects also being observed in the original MusiQoL validation study. Additionally, most of the results were validated by IIC, IDV, and unidimensionality.

In summary, the present study has demonstrated the validity, internal consistency, reproducibility, and acceptability of the Korean versions of the MSIS-29 and MusiQoL questionnaires for patients with MS in Korea. A long-term follow-up study based on the results of this study may provide additional useful information for predicting the HRQoL in Korean MS patients.

**Conflicts of Interest**
The authors have no financial conflicts of interest.

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Table 5. Spearman’s correlation coefficients between dimension scores on the MusiQoL questionnaire and the MSIS-29

| MSIS-29 | ADL | PWB | SYM | RFr | RFa | SSL | REJ | COP | RHS | Index |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|
| PHY     | 0.9 | 0.71| 0.65| -0.01| -0.07| 0.39| 0.48| 0.48| 0.11| 0.78  |
|         |     |     |     |     |     |     |     |     |     |       |
| PSY     | 0.79| 0.84| 0.82| 0.22| 0.14 | 0.35| 0.56| 0.51| 0.31| 0.87  |

ADL: activities of daily living, COP: coping, MSIS-29: Multiple Sclerosis Impact Scale, MusiQoL: Multiple Sclerosis International Quality of Life, MusiQoL Index: global MusiQoL score, PHY: physical impact, PSY: psychological impact, PWB: psychological well-being, REJ: rejection, RFa: relationships with family, RFr: relationships with friends, RHS: relationships with the healthcare system, SSL: sentimental and sexual life, SYM: symptoms.
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