Organ transplant recipients are required to take immunosuppressive drugs for the rest of their life to prevent acute rejection and graft loss. Adherence to this complex, lifelong treatment can be challenging for many patients because of the side effects of the immunosuppressive drugs. These side effects can be evaluated objectively and subjectively.

An objective evaluation involves clinicians’ monitoring for side effects that might have an adverse effect on clinical outcomes, such as nephrotoxic effects, diabetes mellitus, hypertension, and hypercholesterolemia. A subjective evaluation of side effects refers to the patients’ perspectives of immunosuppressive side effects. Traditional objective evaluations do not fully explain how immunosuppressive treatment affects transplant recipients’ life, as subjectively experienced side effects might trigger nonadherence or result in a decreased quality of life. Regular measurement of the patient’s appraisal of the experience and the distress of side effects should be perceived as a key strategy to prevent poor outcomes.

Self-reporting is a method of choice to capture a patient-reported outcome: As it generates information directly obtained from the patient without...
The Modified Transplant Symptom Occurrence and Symptom Distress Scale-59 Items Revised (MTSOSD-59R) is a validated self-report scale that has been developed to assess the presence and distress of side effects associated with the use of both older and newer generation immunosuppressive drugs (ie, corticosteroids, tacrolimus, mycophenolate mofetil, sirolimus, everolimus).16 Advantages of this scale, in comparison to other existing scales, are that this scale is based on a conceptual framework, is comprehensive, and focuses on side effects of immunosuppressive drugs exclusively.5,16

The conceptual framework underpinning the MTSOSD-59R is based on the self-regulation theory, stating that an experience of a side effect or a “symptom” consists of a cognitive component and an emotional component.17 The cognitive component of symptom experience, which can be measured along the dimensions of frequency or severity, is referred to as “symptom occurrence.”17 The emotional component of symptom experience refers to the mental anguish or suffering caused by the symptom, which is labeled as “symptom distress.”17 The MTSOSD-59R scale has been previously validated in Dutch and English languages and adapted in a culturally sensitive way to Hindi, Spanish, Portuguese, French, German, Polish, and Italian.16 It is currently unknown if the MTSOSD-59R would also be suitable for use in Turkish-speaking transplant patients. In the literature, adaptation of the scale to different cultures in different organ transplant recipients is recommended.16,19

Compared with the development of a new scale, adaptation of an existing scale would be more cost-effective, and time-saving, and would allow international comparisons on condition that the items of the scale are understood by patients being treated in a different cultural environment and that the validity of this scale for this new language has been demonstrated.20 The purpose of this study was, therefore, to (1) translate the scale into Turkish in a culturally sensitive way, (2) adapt the scale on the basis of input from patients and experts, and (3) validate the updated version in Turkish-speaking transplant recipients.

Materials and Methods

This project consisted of 4 consecutive phases, of which the methods are described next.

Culturally Sensitive Translation of the MTSOSD-59R Into Turkish

The MTSOSD-59R consists of items about side effects of traditional and novel immunosuppressive drugs and assesses the patient’s appraisal of symptoms associated with side effects of immunosuppressive drugs. Content and construct validities have been described elsewhere.16 Each symptom is scored in view of both symptom occurrence and symptom distress. Symptom occurrence is assessed on a 5-point rating scale ranging from 0 (never occurring) to 4 (always occurring) and symptom distress on a 5-point rating scale ranging from 0 (not at all distressing) to 4 (extremely distressing).

The original instrument was translated into Turkish by the investigators, whose native language was Turkish, but who have a good command of English as they are teaching medical English at the university. Both forward translations were compared and consensus was reached about the most suitable translation. Back translation of the instrument into English was done by 2 people whose native language was Turkish, but who had a good command of both languages and who did not see the English version of the instrument (both were teaching English at the nursing school). The back-translated version was compared with the original scale. Next, 15 liver transplant recipients in the liver transplant outpatient clinic completed the Turkish MTSOSD-59R and were asked to indicate difficulties with the meaning of items or instructions. Suggested changes were incorporated before this scale was used for validity purposes.

Content Validity

To test content validity, a total of 13 experts specializing in organ transplant were asked to evaluate whether each item indeed represented a symptom associated with a side effect of immunosuppressive drugs.

Each item in the instrument was scored on a 4-point scale, with 1 representing “not relevant at all” and 4 representing “very relevant.” Scores 3 and 4 were combined, and a content validity index (CVI) score was calculated. The CVI was used to assess the items’ relevance. CVI is computed 2 ways: item and scale CVI. Item content validity index (I-CVI) was computed for each item and should be greater than 0.78. Scale content validity index (S-CVI) was computed for all items of the scale combined and should be greater than 0.90.21 In the study, the I-CVI and S-CVI of the Turkish MTSOSD-59R were computed. Next, 30 liver transplant recipients in the liver transplant outpatient clinic completed the revised Turkish MTSOSD-59R according to expert opinions and were asked to indicate difficulties with the meaning of items or instructions.

Construct Validity Related to Known Groups

The known-group approach was used to test the construct validity of the instrument. Symptom occurrence and symptom distress are influenced by the sex and depression level of the patients.22,23 Thus, in this
study, evaluation of the known-group approach was based on the sex and the mean depression scores of organ transplant recipients.

The known-group approach was used to evaluate MTSOSD-59R scores of transplant patients taking immunosuppressive drugs compared with patients who were not taking such medications. Symptom levels of transplant patients were expected to be higher than symptom levels in a healthy control group.

Reliability
Calculation of Cronbach α is useful only if the items of the instrument are conceptually related to each other. The items of the MTSOSD-59R are deliberately and appropriately not homogeneous; thus the Cronbach α was not calculated for the original instrument or for symptom occurrence and symptom distress.1,16

We used the split-half technique16 to test the reliability of the Turkish MTSOSD-59R. Items of the scale were divided into 2 sections as odd-number items and even-number items. Then, split-half reliability was evaluated for correlation between single-number items and couple-number items with Spearman-Brown corrected correlation analysis.

Design
We used a cross-sectional design to validate the MTSOSD-59R with respect to known groups’ construct validity. More specifically, 3 known-groups differences, derived from the literature1,13,16 were tested to demonstrate validity: We anticipated that healthy control participants would experience fewer side effects than would patients who were taking immunosuppressive drugs, that female transplant patients would have more symptoms and distress than male recipients, and that patients with depressive symptoms would experience more symptoms than would nondepressed patients.

Participants and Setting
The convenience sample consisted of 180 liver and kidney transplant recipients treated in 2 university hospitals in the western part of Turkey. The recipients included in the study fulfilled the following inclusion criteria: being 18 years or older, able to understand and speak Turkish, and living for more than 3 months after transplant surgery. Transplant recipients who underwent a multiorgan transplant or retransplant were excluded.

In order to test construct validity with respect to known-group differences, we also recruited 180 healthy control subjects from a community health service in western Turkey. Inclusion criteria for control participants were as follows: not receiving immunosuppressive drugs and hence not being familiar with their side effects, being 18 years or older, and being able to understand and speak Turkish. Healthy controls were matched for age and sex.

Variables and Measurement
Data were collected by using a demographic and clinical characteristics scale, MTSOSD-59R, and the Beck Depression Inventory.

Demographic and Clinical Characteristics Scale.
Data about demographic and clinical characteristics were collected by the investigators via chart review and included sex, age, marital status, educational level, cause of end-stage organ disease, and immunosuppressive regimen prescribed.

Modified Transplant Symptom Occurrence and Symptom Distress Scale-59 Items Revised.
Patients completed the Turkish version of the MTSOSD-59R as described earlier.

Beck Depression Inventory. Published reports show that patients with depression had more symptoms than did nondepressed patients.1,13,16 In order to demonstrate construct validity with respect to known groups, we evaluated whether patients with depressive symptoms experienced more symptoms and a higher distress than did patients without depressive symptoms. We used the Beck Depression Inventory, a 21-item self-report scale, to assess presence and severity of depressive symptoms. Each item is scored on a 4-point scale ranging from 0 (absent) to 3 (severe). The total score ranges from 0 to 63. Higher scores indicate more severe depression.25 The Beck Depression Inventory is a reliable and valid instrument to be used in diverse populations, including transplant recipients.1,26 The Beck Depression Inventory was adapted into Turkish in 1998 by Hisli27 and showed acceptable reliability and validity. A score of 17 or higher is suggestive of the presence of a depressive disorder.27 In our study, Cronbach α coefficients were 0.90 for the healthy control participants and 0.89 for the transplant recipients, indicating excellent reliability.

Procedure
Given that the MTSOSD-59R is copyright protected, written permission to conduct this study was obtained from the test developers on October 5, 2009. Ethical approval was obtained from the ethics committees of the medical and nursing schools before the start of this study. Permission for data collection was granted by the medical director at both university hospitals participating in this study. Also, permission was granted by the manager of the Izmir Provincial Directorate of Health to collect data from healthy control participants. All eligible patients received an information leaflet that explained the purpose of the study in
Validation and adaptation of the MTSOSD-59R into Turkish

Descriptive statistics were used to summarize demographic and clinical characteristics. Data were analyzed by using Statistical Package for Social Sciences (SPSS) version 15.0, Microsoft Office Excel 2007, and Minitab.

Content validity of the Turkish version of MTSOSD-59R was tested by requesting opinions of the experts using the “scale content validity index averaging method.”

Given that symptom occurrence and symptom distress are measured at an ordinal level, Ridit analysis was used. A Ridit score reflects the probability that a score observed for an individual randomly selected from 1 group (eg, patients with depression) will be higher than a score observed for a randomly selected individual from another group, namely, a reference group (eg, patients without depression). A Ridit ranges from 0 to 1. For instance, if a Ridit for symptom occurrence of a patient with depression is 0.75, then this indicates that a randomly selected patient will have a 75% chance of having more symptoms than a randomly selected patient from the nondepressed group. If no difference between both groups exists, the Ridit will be 0.5. Overall symptom occurrence and distress score for each patient were computed by calculating Ridit scores over all symptom frequencies and distress items, respectively.

In construct validation of the instrument, the known-group approach was used. Ridit analysis was used to test construct validity. The reference group in this study was the healthy control group of people not taking immunosuppressant medication.

The median total score of the MTSOSD-59R were used in analysis of the known-group approach, and the Mann Whitney U test was carried out to compare male and female transplant recipients for the known-group approach. Transplant recipients were divided into 2 groups according to their mean scores on the Beck Depression Inventory: those with a score less than 17, representing absence or minor depressive symptoms, versus those with a score of 17 or higher, potentially reflecting presence of a depressive disorder. These groups were compared by using the Mann Whitney U test for known-group approach.

Results
Sample Characteristics

The study sample included 180 transplant recipients and 180 healthy people. Of 180 transplant recipients, 100 underwent liver transplant and 80 underwent kidney transplant surgery. Mean age was 43.58 (SD, 11.96) years in the patients and 42.14 (SD, 13.03) years in the healthy control participants. No significant differences between patients and healthy control participants were found in terms of age and sex as expected, given that we matched samples for these variables. Yet, a significantly higher proportion of patients were married, and their educational level was significantly lower than that of the healthy control participants (Table 1).

The transplants were received less than 1 year ago in 28% of patients, between 1 and 2 years in 19% of patients, between 2 and 5 years ago in 37% of patients, and more than 5 years ago in 23% of patients. The most common cause of liver disease was viral hepatitis (39%) and the most common cause of renal disease was hypertension (20%). The immunosuppressant therapies received by recipients are shown in Table 1.

Validity

Content Validity. The content validity index score was 1.0, indicating 100% agreement between the 13 reviewers. Recommendations to remove items or add items were incorporated into the Turkish version of the MTSOSD-59R on the basis of consensus between the experts.

After pilot testing the questionnaire in 30 patients, the following changes in the instrument were made. In the English questionnaire, items are presented in 2 columns: the first column assesses symptom occurrence, the second column assesses symptom distress. For symptom occurrence, response options are presented vertically (ie, each response option is presented on a new line). For symptom distress, an ordinal scale is used, which is graphically depicted in a horizontal fashion. Turkish patients found it confusing that symptom distress was presented in a second column and suggested that we first ask for symptom occurrence and then for symptom distress in a similar fashion.

Also, item 47 was excluded in the Turkish version of the MTSOSD-59R because the liver transplant recipients noted that item 46 “I have felt tired” and item 47 “I have had lack of energy” were very similar.

Construct Validity. A known-groups approach was used to test construct validity of the instrument.

Known Groups Related to Sex. Figure 1 shows the distribution of Ridit scores of the females (symptom occurrence, 0.560; symptom distress, 0.555) and male (symptom occurrence, 0.547; symptom distress, 0.551) transplant recipients for symptom occurrence and symptom distress.

According to the results of Ridit analysis, the Ridit analysis value was greater than 0.7 in 1% of all the transplant recipients, 4% of the female recipients, and 2% of the male recipients for symptom occurrence.
and in 2% of all the transplant recipients, 4% of the female recipients, and 1% of the male recipients for symptom distress. As expected, female transplant recipients experienced a higher symptom occurrence ($P = .01$) and higher symptom distress ($P = .01$) than did male transplant recipients (Table 2).

Transplant recipients with higher scores for depressive symptoms had a significantly higher mean symptom occurrence and symptom distress scores than did transplant recipients with lower depressive symptom scores ($U = 474.000, P = .001$; $U = 404.500, P < .001$, respectively; Table 3).

Transplant patients are expected to have higher symptom levels than healthy controls. Transplant recipients showed significantly higher Ridits of symptom occurrence (0.55) and symptom distress (0.55) than did healthy control participants (Figure 2). The mean symptom occurrence and symptom distress scores of transplant recipients were significantly higher than those of healthy participants ($U = 6495.000, P < .001$; $U = 8846.500, P < .001$, respectively; Table 4). Figure 3 shows the 10 symptoms most frequently reported by organ transplant recipients and the 10 most distressing symptoms reported in rank order by Ridit scores.

Reliability

In split-half reliability analysis, scale items were divided into 2 equal groups as odds and evens, and correlation between test scores in each group were calculated. Spearman-Brown corrected split-half reliability coefficient was 0.92 for symptom occurrence and 0.92 for symptom distress in organ transplant recipients ($N = 180$). These coefficient values were accepted as the bottom limit of the reliability of the whole test. These findings showed us that Turkish MTSOSD-59R is a reliable scale for the Turkish sample.

Discussion

In this study, we performed validation, adaptation, and reliability testing of the MTSOSD-59R adapted for Turkish culture in a sample of organ transplant recipients. The linguistic validity, content validity, construct
Validation and adaptation of the MTSOSD-59R into Turkish

Table 2  Comparison of median symptom occurrence and symptom distress scores between female and male transplant recipients

<table>
<thead>
<tr>
<th>Scale component</th>
<th>Female (n = 79)</th>
<th>Male (n = 101)</th>
<th>Mann Whitney U</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom occurrence</td>
<td>93.32 (24.29)</td>
<td>85.23 (16.24)</td>
<td>3133.500</td>
<td>.01</td>
</tr>
<tr>
<td>Symptom distress</td>
<td>89.24 (23.44)</td>
<td>81.16 (14.27)</td>
<td>3110.000</td>
<td>.01</td>
</tr>
</tbody>
</table>

Table 3  Comparison of median symptom occurrence and symptom distress scores between patients with low versus high depressive symptom scores on the Beck Depression Inventory (BDI)

<table>
<thead>
<tr>
<th>Scale component</th>
<th>BDI score &lt;17 (n = 153)</th>
<th>BDI score &gt;17 (n = 27)</th>
<th>Mann Whitney U</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom occurrence</td>
<td>86.93 (17.79)</td>
<td>112.46 (35.23)</td>
<td>474.000</td>
<td>.001</td>
</tr>
<tr>
<td>Symptom distress</td>
<td>82.93 (16.53)</td>
<td>107.54 (33.50)</td>
<td>404.500</td>
<td>.000</td>
</tr>
</tbody>
</table>

Figure 2  Overall symptom occurrence and symptom distress in transplant recipients and healthy control participants.

CINAHL databases. Dobbels et al\(^6\) addressed the issue of testing content validity in English (United States) and construct validity in Dutch (Belgium). Moons et al\(^1\) did a validity study of MTSOSD-21 items version, and language validity testing has been performed for many languages (in Brazil, Denmark, France, Germany, India, Italy, Poland, Spain, and Sweden).\(^1\)

Linguistic and Content Validity

First, language adaptation of the MTSOSD-59R was carried out for Turkish cultural adaptation. Technical translation is just as important as cultural adaptation in language validity testing.\(^3\) Therefore, the technical translation of MTSOSD-59R to Turkish was done by translation experts and cultural adaptation of MTSOSD-59R was done with pilot testing and by using an experienced translator.

To test the content validity of the scale, a total of 13 experts specializing in organ transplant were asked to comment about whether the items on the MTSOSD-59R were appropriate. The content validity index was used to determine whether the experts agreed, and I-CVI and S-CVI values of the MTSOSD-59R in this study were acceptable.\(^2\) The values indicate a consensus among the experts concerning items of the MTSOSD-59R. Dobbels et al\(^6\) tested the content validity of MTSOSD-59R by using 17 international experts to review it and pilot testing with 24 kidney transplant recipients. Content validity was evaluated by assessing how many patients correctly completed the questionnaire, and 93% of the sample is reported to have correctly completed the MTSOSD-59R.

Construct Validity

The known-group approach was used for construct validation of the scale. This method is the most-used
approach to testing construct validity.\textsuperscript{31} The female transplant recipients had higher Ridit scores for symptom occurrence and symptom distress than did the male transplant recipients. Also, the female transplant recipients had significantly higher mean scores of both symptom occurrence and symptom distress than did the male transplant recipients. These results showed that the MTSOSD-59R has excellent construct validity, according to the known-group approach in Turkish organ transplant recipients. Our results are supported by Dobbels et al,\textsuperscript{16} who used MTSOSD-59R as the construct validity criterion according to sex and depression level in their study, and reported Mann Whitney \textit{U} test results similar to those described in this study.

We found that the transplant recipients had higher Ridit scores and mean scores ($P < .05$) for symptom occurrence and symptom distress than did the healthy control participants. These results showed that the MTSOSD-59R has excellent construct validity in Turkish organ transplant recipients. Dobbels et al did not evaluate differences in symptom occurrence and symptom distress of organ transplant recipients and healthy control subjects.

In our study, the top 10 symptoms in liver and kidney transplant recipients were increasing sweating, feeling restless or nervous, moon face, trembling hands, hair loss, anxiety, mood swings, excessive appetite, muscle weakness, and increasing hair growth. When our results are compared with the results of Kugler et al,\textsuperscript{32} it is apparent that excessive appetite, moon face, fatigue, hair growth, mood swings, muscle weakness, anxiety, and trembling hands are among the most common and distressing symptoms in solid-organ transplant recipients. Also Drent et al\textsuperscript{33} stated that muscle weakness is among the top 10 symptoms in liver transplant recipients. The symptoms with the highest occurrence and highest distress must be determined in

<table>
<thead>
<tr>
<th>Scale component</th>
<th>Organ transplant recipients (n = 180)</th>
<th>Healthy control participants (n = 180)</th>
<th>Mann Whitney $U$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom occurrence</td>
<td>88.78 (20.51)</td>
<td>73.95 (19.60)</td>
<td>6495.000</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Symptom distress</td>
<td>84.75 (19.23)</td>
<td>75.04 (19.47)</td>
<td>8846.500</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Figure 3  The most frequently occurring and most distressing 10 signs and symptoms among transplant recipients (healthy control group reference Ridit = 0.50).
a larger sample that includes other solid-organ transplant recipients. Besides, such research is needed to determine the factors that affect the symptoms experienced by organ transplant recipients. The results will throw light on care of organ transplant recipients for special organ transplant nurses.

In this study, the reliability of the MTSOSD-59R was evaluated by using split-half reliability analysis for the first time. Also, the Turkish MTSOSD-59R was found to be a reliable scale.

Limitations
Because the study sample comprised only liver and kidney transplant recipients, generalization of the results to other transplant populations is not yet appropriate. Clinical use of MTSOSD-59R is difficult because the number of items is too great.

Conclusion
This study examined the validity of the MTSOSD-59R in Turkish organ transplant recipients. The results suggest that the MTSOSD-59R has appropriate language, content, and construct validity in Turkish organ transplant recipients. This scale can be used to determine symptom occurrence and symptom distress related to immunosuppressive therapy of Turkish organ transplant recipients. Nurses and other health professionals can use it to determine appropriate interventions for prevention, early assessment, and treatment of symptoms related to immunosuppressive therapy. Also, the scale can be used to test the effectiveness of these interventions.

This scale could be used for systematic assessments of patients’ appraisal of side effects of immunosuppressive therapy during clinical follow-up after transplant. The assessment is a very important issue because high-level symptoms are considered as risk for noncompliance.

It is required that the MTSOSD-59R should be summarized and divided into subscales according to immunosuppressive therapy used in clinical practice. Also, because it is difficult to use and understand Ridit analysis, mean scores can be used in evaluation of the MTSOSD-59R.

Acknowledgements
The authors thank the patients who readily agreed to participate in this study and Professor Dr Fabienne Dobbels for her ideas to write the manuscript. Also, we would like to thank Professor Dr Sedat Karademir, president of the transplant institute, Associate Professor Dr Tarkan Üneş, surgeon at the liver transplant center, and Dr Aylin Bacakoğlu, responsible physician in the liver transplant outpatient clinic for supporting the data collection process in this study.

Financial Disclosures
None reported.

References
Ordin et al


