Validity and reliability of Turkish version of quality-of-life questionnaire in adult patients with common variable immune deficiency

Deniz Eyice[1], Semra Demir[1], Halim İşsever[1], Osman Ozan Yeğit[1], Ali Can[1], Özdemir Can Tüzer[1], Pelin Karadağ[1], Nida Öztop[1], Şengül Beyaz[1], Bahauddin Çolakoğlu[1], Suna Büyüköztürk[1], Federica Pulvirenti[2], Isabella Quinti[3], and Aslı Gelincik[1]

[1]Istanbul University Istanbul Faculty of Medicine
[2]Umberto I Polyclinic of Rome
[3]University of Rome La Sapienza

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Abstract

Background and Aims Common variable immunodeficiency (CVID) can affect quality of life (QoL) which can be better assessed with validated scales. Our goal was to validate the Turkish version of the Italian CVID-QoL questionnaire. Methods International recommendations for cultural adaptation and translation process of original scale was followed. CVID patients completed Turkish CVID-QoL questionnaire between October 2019 and January 2020. The Short Form Health Survey (SF-36) was used as a comparative questionnaire. Reliability, reproducibility, factor analysis, content validity, convergent validity and discriminant validity were analysed. Results 50 CVID patients were included in the study. 64 % of patients (n=32), the mean age of the patients was 36.68 ± 13.2 years, the median duration of disease was 52.5 months. The instrument had good internal consistency in 50 patients [Cronbach's alpha: 0.92, emotional functioning (EF): 0.91, relational functioning (RF): 0.77]. It also revealed high reproducibility in 26 patients QoL global, intraclass correlation coefficient (ICC)= 0.80 (95 % CI 0.56 - 0.91); EF, ICC = 0.78 (95 % CI 0.51- 0.90); RF, ICC = 0.82 (95 % CI 0.59-0.92); Gastrointestinal and skin symptoms (GSS), ICC = 0.89 (95 % CI 0.76-0.95); (p <0.001, p <0.001, p <0.001, p <0.001). QoL global, EF and RF scores showed good convergent validity with similar subscales of SF-36. The number of infections within last 3 months had a significant impact on QoL global, EF and RF (p=0.038, p=0.045, p=0.028). Conclusions The Turkish version of CVID QoL scale has appropriate validity and reliability among Turkish patients with CVID.

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Running Title: Quality of life

Deniz Eyice[1], Semra Demir[1], Halim İşsever[2], Osman Ozan Yeğit[1], Ali Can[1], Özdemir Can Tüzer[1], Pelin Karadağ[1], Nida Öztop[1], Şengül Beyaz[1], Bahauddin Çolakoğlu[1], Suna Büyüköztürk[1], Federica Pulvirenti[3], Isabella Quinti[4], Aslı Gelincik[1]

1 Department of Internal Medicine, Division of Immunology and Allergic Diseases, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

2 Department of Public Health, Faculty of Medicine, Istanbul University, Istanbul, Turkey

3 Department of Infective Diseases and Internal Medicine, University Hospital Policlinico Umberto I, Rome, Italy

4 Department of Molecular Medicine, Sapienza University, Rome, Italy

Corresponding author: Aslı Gelincik

Department of Internal Medicine, Division of Immunology and Allergic Diseases Istanbul University, Istanbul Faculty of Medicine, Turgut Özal Millet Cad, 34390, Fatih, Istanbul

gelincikasli@hotmail.com

GSM: +905422370665

Abstract

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Common variable immunodeficiency (CVID) can affect quality of life (QoL) which can be better

assessed with validated scales. Our goal was to validate the Turkish version of the Italian CVID-QoL questionnaire.

Methods

International recommendations for cultural adaptation and translation process of original scale was followed. CVID patients completed Turkish CVID-QoL questionnaire between October 2019 and January 2020. The Short Form Health Survey (SF-36) was used as a comparative questionnaire. Reliability, reproducibility, factor analysis, content validity, convergent validity and discriminant validity were analysed.

Results

50 CVID patients were included in the study. 64 % of patients (n=32), the mean age of the patients was 36.68 ± 13.2 years, the median duration of disease was 52.5 months. The instrument had good internal consistency in 50 patients [Cronbach's alpha: 0.92, emotional functioning (EF): 0.91, relational functioning (RF): 0.77]. It also revealed high reproducibility in 26 patients QoL global, intraclass correlation coefficient (ICC)= 0.80 (95 % CI 0.56 - 0.91); EF, ICC = 0.78 (95 % CI 0.51- 0.90); RF, ICC = 0.82 (95 % CI 0.59-0.92); Gastrointestinal and skin symptoms (GSS), ICC = 0.89 (95 % CI 0.76-0.95); ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$). QoL global, EF and RF scores showed good convergent validity with similar subscales of SF-36. The number of infections within last 3 months had a significant impact on QoL global, EF and RF (p=0.038, p=0.045, p=0.028).

Conclusions

The Turkish version of CVID QoL scale has appropriate validity and reliability among Turkish patients with CVID.

Keywords: common variable immune deficiency, quality of life, scale validation, linguistic validation

Introduction

Common variable immunodeficiency (CVID) is the most frequent and commonly diagnosed symptomatic primary immune deficiency disorder in adults [1] with prevalence ranging from 1 in 10 000 to 1 in 50 000 in different populations [2]. CVID is characterized by various clinical conditions such as severe infections, malignancy, granulomatous and autoimmune disorders [1]. Although some patients have symptoms from early childhood, the distinguishing feature of CVID is primary hypogammaglobulinemia caused by late onset antibody failure [3]. Immunoglobulin (Ig) replacement is the main treatment for the prevention of recurrent infections, and it can decrease frequency of bacterial infections however, it is less effective on other CVID associated complications[4, 5].

Patient-focused assessment methods have become more important in the follow-up of the patients with chronic diseases [6]. In addition, this approach strengthens the relationship between the doctor and the patient, makes some problems visible that are not noticed routinely and enables better follow-up of diseases and treatments[7]. In very few studies analysing the psychosocial aspects of CVID, patients are not homogenous group as shown for other chronic diseases [8]. In addition, there is a lack of knowledge about one of the rare diseases CVID which has different psychological and social effects both in society, individuals and healthcare providers [9]. In recent years, with considerable progress in early diagnosis, increased awareness and Ig replacement therapy led to a significantly extended life expectancy for patients with primary antibody deficiencies[10].

Ever since the World Health Organization defined health not only as the absence of disease and illness, but also as the presence of physical, mental and social well-being, questions of quality of life have become increasingly important in health practice and research[11]. In healthcare, QoL is an assessment of how different aspects of an individual's life can be affected by a disease or a disability [12]. It is a comprehensive concept that is important to evaluate the impact of disease, treatment and symptoms[13]. QoL is an important health outcome representing the ultimate goal of all health interventions and the use of valid and reliable measurements is essential for providing evidence-based health care [14].

Clinicians mostly deal with more objective data of their patients and whether their illness is cured. QoL scales are mostly used for research purposes and are very rare examples in routine clinical practice. There are many different quality of life scales that contain questions about different aspects of life (environment, social, economics, etc...) that can be used with patients and healthy populations [14]. The tools for measuring QoL can be divided into 2 groups: generic and specific. Generic scales can be applied to all kinds of patients and healthy groups including general questions that are not specific to the disease. Specific scales focus on a group or single illness or symptom[15]. Because generic QoL scales may not capture the positive and negative effects of some specific limitations and effects of each disease and each disease may have specific clinical features and mental effects, it is more appropriate to use validated disease-specific scales.

The measurement of health-related quality of life (HRQoL) in primary immunodeficiency has arisen relatively recently from an effort to document the outcome of therapeutic intervention and the need to obtain information about patients' well-being as well as objective findings visible to physicians [16]. On the other hand, CVID manifestations which are the findings of more common diseases and have been frequently investigated but the knowledge about the effects of Ig replacement therapy on patients is insufficient. Thus, development and validation of a disease-specific HR-QoL survey tool and researchers' understanding of the quality of life of CVID patients is necessary.

In previous studies, generic health status QoL scales were used such as Short form (SF-36, SF-12) and General Health Questionnaire (GHQ-12) in adult CVID population [16-18]. The need for a specific QoL scale that includes better questions has arisen because it can provide the features of CVID more accurately. Quinti et al developed the CVID specific QoL questionnaire in 2015 [10] and it was used in scientific studies in Norway and Italy [19, 20].

The aim of this study was to translate this Italian CVID QoL scale to Turkish and investigate the validity and usefulness of CVID QoL questionnaire and determine the impact of CVID on quality of life for use with adult CVID patients by healthcare professionals and researchers.

Methods

Characteristics of the instrument

The Italian version of CVID-QoL is developed by Quinti et al. in 2015[10]. It consists of 32 items that are most predictive of self-care behaviours, patients' aspects of the Ig replacement therapy and the features of CVID. The questionnaire is designed to review the situation for the last 3 months. The instrument is a 5-point-likert scale with 0= "never", 1= "rarely", 2= "sometimes", 3= "often" and 4= "always" with higher values generally indicating increasing disability. Total score ranges from 0 (minimum score) to 128 (maximum score); higher

scores indicate poorer QoL. It was also identified in percentages as the ratio of the QoL score to the maximum score.

Instrument translation of CVID QoL

To ensure a linguistic equivalence with the original questionnaire, the cross- cultural validation process was conducted according to an international consensual systematic methodology, called standardized linguistic validation[21, 22]. Permission to translate and validate CVID QoL into Turkish language was obtained from the original questionnaire developer (Dr Pulvirenti and Dr Quinti, author on this manuscript). Two separate forward translations from Italian to Turkish involving two independent both bilingual but native speakers were conducted, and they were reconciled into one version. Then the backward translation of the reconciled version into Italian was made by native speakers. The backward translation was compared with the original Italian questionnaire by the expert committee. Afterwards the pre final Turkish version of questionnaire was obtained. (Figure 1.) In this version, the content validity index was determined for each item by ten experts by using the options of 1= "not suitable", 2= "partially suitable, applicable by modification", 3= "the item available as it is". After this step, the Turkish version of the questionnaire was applied individually to five eligible patients as a pilot study. Meanwhile, we got their comments on whether all 32 items were understandable and suggestions for changes. Finally, the last version CVID QoL was approved.

Patient selection

This methodological study was conducted in Istanbul University, Faculty of Medicine, Adult Immunology and Allergy Clinic. To be included in the study, all of the following inclusion criteria had to be fulfilled: >18 years, diagnosis of CVID more than 6 months, currently receiving intravenous or subcutaneous immunoglobulin replacement therapy. CVID was diagnosed according to the ESID criteria[23]. Inability or unwillingness to give informed consent and significant medical or psychiatric illness were the exclusion criteria.

Procedures

Demographic and clinical characteristics were recorded: age, gender, education level, number of infections experienced within the 3 and 12 months before participation (self- reported), disease duration, Ig levels at the time of diagnosis, the last IgG trough levels, current body mass index, route of Ig administration.

We used the short form health survey (SF-36) as a comparative questionnaire. It is a self- administered questionnaire, including 36 items Likert type or multiple-choice scale which has 8 different dimensions; physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health[24]. Scores for each dimension range from 0 to 100, with higher scores indicating better health.

Patients were asked "How severe is your disease?" Answers were given on a 5-point scale from 0: "very mild," 1: "mild," 2: "moderate," 3: "severe," and 4: "very severe." The patient general assessment (PtGA) was completed before meeting the physician as were other two questionnaires. At the end of the visit, physicians also evaluated the disease severity of each patient with physician general assessment (PhGA) with the same 5- points.

Factor analyses was evaluated both QoL scores and percentages to ensure the accuracy of the analyses.

The Turkish version of CVID QoL was applied to the participants 14-21 days after the first evaluation to prove the reproducibility.

The institutional review board and the Ethics Committee of Istanbul University, Faculty of Medicine approved the study (149, 2019/ 1453) and informed consent was obtained from all study participants.

Statistical analyses

Statistical data analysis was performed using SPSS.21 version. Normality analysis showed that all continuous variables for all groups did not confirm normal distribution. Categorical variables were summarized as frequencies and percentages; continuous variables were given by using means and standard deviations

when normally distributed, median (min-max) when abnormally distributed. Two measures of reliability were included: internal consistency and test–retest reliability. Internal consistency was tested using Cronbach's alpha for the patient group. Test–retest reliability was carried out using Intraclass Correlation (ICC). Construct validity was assessed by estimating Spearman's correlation coefficients between the subscales of the CVID QoL TR and the items of the SF-36. Additionally, Mann- Whitney U test and Kruskal- Wallis test was conducted to evaluate the discriminant validity of the tool.

Results

Demographic and clinical findings of the study participants

50 patients with confirmed diagnosis were enrolled in the study between October 2019 and January 2020. The majority of the patients were males (64%), the mean age of the patients was 36.68 ± 13.2 years, 88 % of patients (n=44) were younger than 50 years of age and 56 % (n=28) had a body mass index (BMI) within the normal range. 56 % of patients (n=28) had less than 13 years of education. The median duration of disease of the patients was 52.5 (6-384) months. The majority of the patients 86 % (n=43) received IVIG treatment. The median number of reported infections within 3 and 12 months before the participation of the test was 1 (min-max: 0-3) and 3 (min-max: 0-12), respectively. The main clinical and demographic features are summarized in Table 1.

Content validity

To establish consensus for content validity beyond the standard error of proportion ($P < 0.05$) the content validity index (CVI) required was [?]0.70. In the first evaluation of ten experts our CVI was 0.80 for the initial 32 items while 26 of them scored an acceptable CVI for inclusion. The remaining 6 items were discussed, missing concepts identified and a final CVI employed to determine inclusion. Afterwards it was applied to the pilot group(n=5). They reported all 32 items were clear, understandable and applicable. Later, we started the study process that we applied the questionnaire to 50 patients.

Feasibility

50 patients completed the questionnaire in approximately 10-15 minutes. Our missing response rate was 0.25 % for all questionnaire items. 3 patients left the *item 23* blank which was about sexuality.

Reliability

High internal consistency was found for all questions (QoL Global) with Cronbach's alpha value 0.92. The EF (emotional functioning) and RF (relational functioning) subscales also had good internal consistency with Cronbach's alpha value 0.91 and 0.77 respectively. GSS subscale consists of 4 items and the Cronbach's alpha value was 0.47 when considering all these 4 items. But when we considered only *items 4 and 14* which directly deal with bowel symptoms, Cronbach's alpha value was 0.80.

Convergent validity

Correlations between the dimensions of CVID QoL and SF-36, PtGA, PhGA were shown in Table 2. QoL global, EF and RF scores showed good and moderate correlations with similar dimensions of SF-36. Three dimensions and QoL global showed good correlation with PtGA and the correlation between PtGA and PhGA was also significant (r value =.541, p< 0.001). Physical component summary (PCS) and mental component summary (MCS) total scores also showed good correlation with the QoL scores. (r=-.781, p<0.001; r=-.778, p<0.001).

Discriminatory validity

Comparison of the patients' QoL scores percentages with the number of infections within 3 months and 12 months is summarized in Figure 1. Patients who experienced more than 1 infection within 3 months had significantly higher scores of QoL global, EF and RF (p=0.038, p=0.045, p=0.028). Although the number of infections within the 12 months was not statistically different (p=0.108, p=0.106, p=0.230), we observed that those who had more infections had higher QoL global, EF and RF scores (Figure 2).

Reproducibility

The instrument was re-applied to 26 patients of the participants 14-21 days later. There were no significant differences in the first and second evaluation. QoL global, ICC = 0.80 (95 % CI 0.56 - 0.91); EF, ICC = 0.78 (95 % CI 0.51- 0.90); RF, ICC = 0.82 (95 % CI 0.59-0.92); GSS, ICC = 0.89 (95 % CI 0.76-0.95) ;(p <0.001, p <0.001, p <0.001, p <0.001).

Floor and ceiling effects

Overall, 43.8 % (n=700) of all replies was '0=never' and 5.5 % (n=88) was '4=always'. The lowest score (the best QoL score) of the whole group was 1 in 1 patient. The highest score (the lowest QoL) was 89 in 1 patient. The 25th and 75thpercentile of the QoL global was 21 and 51.5. The questions most frequently answered as 'often' and 'always' ([?] 30 % of the entire group) were related to cough, difficulty in usual activities, tired, fear of illness, becoming infected. The questions answered as 'never' were about fear of death, troubled by other patients, limited by cough, contagious by [?] 70 % of the entire group

Factor analysis

In the current study, factor analysis did not show the 3 factors structure (EF, RF, GSS) as determined in the index study. For GSS subscale, *item 4* and *item 14* related with the bowel symptoms were distinguished from the *item 2 'dietary changes'* and*item 26 'skin symptoms* . In RF subscale, *item 11 'run out of medications'* and *item 16 'as contagious'* , *item 6 'cough'*and *item 25 'limitation of leisure activity'* were distinguished from the other items in the RF dimension.

General QoL assessment of the patients

We observed that the median QoL scores in all patients group was 32 (min-max: 1-89). Female participants reported higher QoL scores indicating poor QoL (p= 0.009). The patient group with less than 13 years of education had higher QoL scores compared to the group with more than 13 years of education (p= 0.015). Higher QoL scores were also observed in the IVIG treatment group when compared to the SCIG treatment group (p= 0.005). We did not observe significant correlation between age, BMI, duration of disease and QoL scores (p>0.05). The QoL scores of our patients and Italian and Norwegian groups were given according to gender, age, education, IVIG, SCIG and BMI groups in Table 3.

Discussion

In Turkey, standardized QoL tool for the assessment of disease burden in CVID patients is lacking. In the current study which had high response rate and positive response from CVID patients we validated the Turkish version of CVID QoL questionnaire and its psychometric properties. It showed excellent reliability, good content validity and reproducibility.

Concerning reliability, our results revealed that all items had excellent internal consistency (>0.9) and 2 subscales, EF and RF exhibited good internal consistency as well (>0.7). These findings are in agreement with the results (0.82, 0.84) of the original Italian version [10] and similar (0.91, 0.77) to the Norwegian cultural adaptation study [19]. The GSS subscale did not achieve the acceptable internal consistency. It consists of only 4 items, 2 of them are related to the diarrhea, 1 skin diseases and 1 dietary change and these 4 elements were not very related to each other. This may be one of the reasons for the low internal consistency. When we consider only two items (4 and 14) which directly deal with bowel symptoms, it exhibited good internal consistency similar to the findings of the Norwegian study [19]. Another possible reason we considered was that our sample group was small to establish construct validity [25]. In addition, cutaneous problems are not seen as often as gastrointestinal manifestations. Generally autoimmune skin problems and case based cutaneous diseases are seen [26-28]. On the other hand, Ballow et al. developed and published a new disease specific tool for primary antibody deficiencies. It did not include any question about skin problems [29]. Therefore, we may consider that dermatologic features do not have an important impact on QoL of CVID patients, but more comprehensive studies are necessary to indicate this. Additionally, similar to the findings from the index study and cultural adaptation [10, 19] test–retest reliability results indicated that the Turkish

CVID QoL scale (CVID QoL TR) also exhibits excellent short-term stability. This indicated that outcomes from the CVID QoL TR were reproducible, supporting its potential use as a patient-reported outcome tool.

Content validity is the ability of a tool to determine the area of interest and the conceptual definition of a structure[25]. During the determination of content validity, we found our CVI was acceptable. But the content validity ratio could not reach the value of 0.7 in 6 items for at the first stage. Minor changes were then made in the 6 items and the main structure was maintained. The last version of tool was approved. We considered that these findings contributed to the content validity.

Convergent validity assesses the extent to which a questionnaire/ tool measures what it is designed to measure [30]. It is estimated by correlating its items with other validated questionnaires measuring the same or similar constructs. To examine the convergent validity of the CVID-QoL-TR, we used SF-36 as a comparative tool. SF-36 is a well-known general QoL scale, translated and validated in Turkish language and used in various diseases [31, 32]. Good correlations were found between QoL global, EF and RF subscales of the CVID-QoL-TR with certain items of the SF-36. CVID QoL scores correlated strongly with both SF-36's physical and mental health domains. Quinti et al. showed good convergent validity for the EF and RF subscales correlating with conceptually similar dimensions of SF-36[10]. Andersen et al. reported the similar findings with/to WHQOOL BREF[19]. Discriminant validity is a statistical concept assessing the ability of a tool/questionnaire to detect true differences and discriminate between the other tools or changes. It indicates that the two things/measure that should not be related are actually irrelevant [25]. Our results showed that the QoL, EF, RF scores were higher in the patients complaining of more than one infection within 3 months before the study. Quinti et al reported that the frequency of infections both within 3 months and 12 months before the study had an impact on the quality of life. We did not observe this association within 12 months before the study. We can speculate that this might be related to the questionnaire seeking answers to questions about the last 3 months and 12 months is a longer duration to recall.

Factor analysis is a multivariate statistics that obtains to find a small number of conceptually significant new variables (factors, dimensions) by combining a large number of related variables intended to measure the same structure or a particular property[33, 34] More accurate factor analyses stated that sample size should have at least 3-5 times more number of items [35]. In the current study, we could not verify the factor analysis since our sample size did not have large number of participants. However, we could perform factor analysis for GSS and RF subscale because they have 4 and 9 items respectively. We observed GSS subscale *item 4* and*14* related with the bowel symptoms were distinguished from the*item 2* 'dietary changes' and *26* 'skin symptoms. In RF subscale, *item 11* 'run out of medications' and *item 16* 'as contagious', *item 6* 'cough' and *item 25* 'limitation of leisure activity' were distinguished from the other items in the RF dimension. But EF and QoL had more items than 50-participant-group could verify these factors. Although factor analysis does not confirm 3 factors. Good correlation with SF 36, reliability, reproducibility and high response rate showed us that CVID QOL TR is a useful scale. We can believe that factor analysis can be re-evaluated as the instrument will be used in the future.

We observed that being female were negatively associated with QoL. This finding was similar to the information of other CVID QoL studies[10, 16, 18]. Receiving IVIG treatment was the second factor associated with poor QoL, it was also consistent with the previous studies[10, 16]. We observed better quality of life in the patient with more than 13 years of education similar to the findings of the Italian and Norwegian group. We did not observe any association between BMI, age and QoL in our study. It might be related to the ethnic differences. Generally, we could not compare directly the findings of our study between the Italian and Norwegian study groups. Our QoL scores did not normally distributed, but the Italian and Norwegian groups showed that their findings were normally distributed (Table 3.) Our study group achieved similar mean CVID QoL scores with Norwegian group while higher than Italian group. 43.7 % of all replies were 0 and our floor and ceiling effects showed better QoL. Since these effects were not evaluated in the index study so we could not compare the findings totally. Differences in the results of our study group between the other groups may be explained with the variation in the demographic features of the study groups. Our study group had higher proportion of male and younger patients as well as the education levels of our

patients were lower than the participants of other study groups. Furthermore, it might be associated with low socioeconomic status or other cultural differences that could not be differentiated in the disease specific tools. CVID QoL instrument is a disease specific questionnaire. It could not measure the impact the social requirements or economic or psychologic situations. Finally, we believe it is not suitable for comparison.

Our study had some limitations. One of them was the low number of adult CVID patients included in the study though we are one of the largest centres in Turkey. Therefore, the analysis could not be properly done to verify the factor analyses and structural validity. Second, there is also the possibility of recall bias, since patients were asked to report on their health in the past 3 months.

In conclusion, CVID disease specific questionnaire is necessary to better evaluate the disease burden on the patients Our study indicated that Turkish version of CVID QoL questionnaire was a reliable, useful and valid instrument for the measuring of quality of life in CVID patients. It is recommended to investigate its stability by applying it to larger patient groups and further consideration on factor analysis. In addition to that, future evaluation of QoL in CVID either with this CVID QoL TR in other Turkish patients or also other translations to other languages can facilitate the improve the knowledge about CVID disease burden on individually.

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Conflicts of interest

Authors state that there is no conflict of interest about this study.

Table 1. Main demographic and clinical features compared with the index study

	Turkey n=50	**Italy n=118**
Demographic characteristics		
Female/Male (n)	18/32	72/46
Age, years (mean ± SD)	36.68 (13.2)	NA
Age [?] 50 years (n, %)	44 (88)	66 (56)
Age > 50 years (n, %)	6 (12)	52 (44)
Education [?] 13 years (n, %)	25 (50)	31 (26)
Clinical characteristics		
IVIG (n, %)	43 (86)	105 (89)
SCIG (n, %)	7 (14)	13 (11)
BMI [?] 18.5 (n, %)	6 (12)	9 (7)
BMI 18.6- 24.9 (n, %)	28 (56)	67 (57)
BMI [?] 25 (n, %)	16 (32)	42 (36)
Disease duration, months (median, min-max)	52.5 (6-384)	NA
Number of infections within 3 months (median, min-max)	1 (0-3)	NA
Number of infections within 12 months (median, min-max)	3 (0-12)	NA

SD: standard deviation, IVIG: intravenous immunoglobulin, SCIG: subcutaneous immunoglobulin, BMI: body mass index, NA: not available

Table 2. Correlations of the CVID QoL scores with the SF-36

	CVID QoL Global	**Emotional functioning**	**Relational functioning**	**Gas**
SF-36				
Physical functioning	-,554**	-,504**	-,461**	-,49
Role-physical	-,613**	-,631**	-,472**	-,28
Bodily pain	-,564**	-,582**	-,550**	-,26
General health	-,533**	-,541**	-,456**	-,25
Vitality	-,535**	-,551**	-,394**	-,46
Social functioning	-,730**	-,713**	-,666**	-,34
Role-emotional	-,503**	-,517**	-,372**	-,30
Mental health	-,606**	-,607**	-,498**	-,40
Physical component summary (PCS)	-,781**	-,789**	-,655**	-,40
Mental component summary (MCS)	-,778**	-,782**	-,639**	-,47
GA				
PhGA	,351*	,300*	,365**	,047
PtGA	,782**	,758**	,744**	,337

QoL: Quality of life, SF-36: short form-36, GA: general assessment, PhGA: physician general assessment, PtGA: patient general assessment

***. Correlation is significant at the 0.01 level (2-tailed).*

**. Correlation is significant at the 0.05 level (2-tailed).*

Table 3. Comparisons of the CVID QoL scores between the Turkish, Italy and Norway study groups

Characteristics	Global CVID QoL scores	Global CVID QoL scores	Global CVID QoL scores
	Scores, median (min-max) Scores, mean (± SD)	Scores, mean (± SD)	Scores, mean (± SD)
	Turkey n=50	Italy n=118	Norway n=83
Total	32 (1-89) 36.4 (20.7)	29 (16.5)	37.4 (15.3)
Female	45 (11-89) 47.38 (21.4)	31.3 (16.4)	38.6 (15.6)
Male	27 (1-66) 30.2 (17.8)	25.7 (14.2)	33.8 (14.4)
Age [?] 50 years	33 (1-89) 37.3 (20.8)	26.5 (15.5)	37.7 (17.9)
Age > 50 years	24.5 (8-61) 29.8 (20.7)	32.6 (15.7)	37.1 (11.8)
Education [?] 13 years	43 (4-89) 43.1 (21.7)	32.1 (17.5)	37.6 (18.8)
Education > 13 years	26 (1-68) 29.6 (17.6)	28.3 (15.3)	37.2 (12.1)
SCIG	21 (4-27) 17.7 (8.4)	*NA*	41.1 (15.7)
IVIG	37 (1-89) 39.4 (20.6)	*NA*	34.5 (13.5)
BMI [?] 18.5	38.5 (21-79) 45 (22.8)	41.1 (11.4)	39.3 (3)
BMI 18.6-24.9	31 (1-89) 35.7 (21.1)	28.2 (15.8)	37 (16.2)
BMI [?] 25	35 (4-68) 34.3 (19.7)	28 (15.9)	35.5 (15.2)

CVID QoL scores are presented as median (min-max) and mean (SD) in Turkish study group, mean (SD) in Italian and Norwegian group. *Abbreviations; CVID: common variable immunodeficiency, SD: standard deviation, SCIG: subcutaneous immunoglobulin, IVIG: intravenous immunoglobulin, NA: not available*

Figure legends

Figure 1. Flowchart of the stages of cross-cultural adaptation and content validation of CVID QoL

Abbreviations; T1-T2: first and second translations from Italian to Turkish, CVID: common variable immune deficiency

Figure 2. Number of infections and CVID QoL, EF, RF, GSS scores. Patients were divided according to the number of infections within 3 months (**A**) and within 12 months (**B**). P values of CVID QoL global, EF, RF scores within 3 months between 0-1 infection and >1 infection were 0.038, 0.045, 0.028 respectively. P values of CVID QoL global, EF, RF scores within 12 months between 0-2 infections, 3-6 infections and >6 infections were p>0.05.

Abbreviations: CVID, common variable immune deficiency; EF, emotional functioning; RF, relational functioning; GSS, gastrointestinal and skin symptoms; QoL, quality of life.

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`Tables.docx` available at https://authorea.com/users/384981/articles/712723-validity-and-reliability-of-turkish-version-of-quality-of-life-questionnaire-in-adult-patients-with-common-variable-immune-deficiency