Common Variable Immunodeficiency Quality of Life Questionnaire: translation and validation into Portuguese

Questionário de Qualidade de Vida na ICV: tradução e validação em português

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To the Editor,

Common Variable Immunodeficiency (CVID) is the most prevalent symptomatic primary immunodeficiency in adulthood. CVID patients are particularly susceptible to infections and immune dysregulation, which significantly contribute to the overall disease burden (1, 2, 3).

Quality of life (QoL) has been increasingly valued in the management of CVID. In 2016, Quinti *et al.* developed and validated a questionnaire to assess CVID-specific health-related QoL in adulthood (CVID_QoL). It is a self-reported tool, originally developed in an Italian cohort to evaluate emotional functioning - EF (19 items assessing patients' subjective status and complaints); relational functioning – RF (9 items focusing on patients' interactions with relatives/individuals without CVID), and CVID-related clinical manifestations, namely gastrointestinal and skin symptoms - GSS (4 items). Answers to these 32 items are rated on a 5-point scale, resulting in a CVID_QoL

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Global score ranging from 0 to 128, which is expressed as a percentage. Higher scores are associated with more severe impairments (2).

Translation into Portuguese and linguistic validation of the *CVID-PT_QoL* strictly followed Quinti *et al.* recommendations (2): Phase 1, two native Italian translators produced independent Portuguese versions that were then combined in a final version; Phase 2 (back-translation), two other independent translators retranslated this Portuguese version back into Italian, without access to the original Italian version. The Portuguese version was then reviewed by two clinicians who follow CVID patients. In Phase 3, the questionnaire was applied to five patients to evaluate their interpretation and comprehension, resulting in a final version of CVID-PT_QoL (Fig. 1).

The validated *CVID-PT_QoL* was then applied to a randomly selected group of 53 Portuguese CVID patients who were followed in a tertiary center. In parallel, epidemiological and clinical data were collected and two other questionnaires were applied: the *Medical Outcomes Study in the Short Form 36* questionnaire (SF-36), including 36 multiple-choice items designed to measure the mental component (MC) and the physical component (PC), with higher scores associated with better health; and the *Hospital Anxiety and Depression Scale* questionnaire (HADS) (3,4,5).

CVID patients were predominantly females (64%), with a mean age of 46±13years, and were mostly under intravenous immunoglobulin replacement (77%). An overall compromised QoL was obtained with *CVID-PT_QoL* (29.4±16.5) (Table 1). We found no significant correlations between *CVID-PT_QoL* and patients' educational level, current age, age at diagnosis, duration of illness, or age at beginning of IgG replacement therapy. Interestingly, we observed similar global *CVID_QoL* and subscale scores as compared to the Italian cohort (*CVID-PT_QoL,* EF:32.4±17.5%; RF:17.5±32.4%; GSS: 26±21%) (2).

The presence of chronic diarrhea significantly affected the CVID_QoL global score in our cohort, as previously reported in the Italian cohort (p = .004).

In addition, we found that patients reporting infections in the 3 months preceding the study (n = 33) experienced a significant negative impact on the Global CVID-PT_QoL score (p = .045), with no other significant differences observed when stratifying patients according to other clinical manifestations.

Regarding the results of the applied complementary questionnaires, impaired physical and low emotional functioning were identified in CVID patients, as indicated by the SF-36 (PC summary: 50.0±18.5 and MC summary: 60.2±3.4). We observed a significant correlation between CVID-PT_QoL and SF-36, particularly in mental health domains. The strongest correlation was observed between the *CVID-PT_QoL* Global score and the SF-36 MC summary dimension (r=-.828, p<.001) (Fig.2).

Curiously, HADS identified patients with severe anxiety (n=9, 17%) and/or severe depression (n=4, 8%). Patients reporting severe anxiety symptoms presented significantly poorer scores compared to other CVID patients, both in the Global CVID-PT_QoL (mean 43.1±14 vs 26.6±15.7; p < .009) and in the dimensions of EF (p = .04) and GSS (p = .0037). Similarly, patients reporting severe depression symptoms also presented with worse scores compared to the other patients: Global CVID-PT_QoL (mean 46.6±14 vs 27.4±15; P < 0.0007); dimensions EF (p = 0.01), GSS (p = 0.0002), and RF (p = 0.013). The question of whether mental health might have influenced self-perception of QoL or if these traits may reflect a heavy burden of disease remains open to debate (1,2,3).

We also found significantly poorer quality of life scores in patients under intravenous IgG (IVIG) replacement. An eventual bias in these results may reside in the fact that patients undergoing IVIG presented a more severe clinical phenotype, as suggested by significantly lower SF-36 Physical Component scores (Table 1). We also hypothesize that the burden of the hospital setting and longer duration of IVIG treatment have a negative impact on patients' QoL and Emotional Functioning, as supported by significantly higher Emotional Functioning and SF-36 Mental Component scores (Table 1).

Table1. Demographic, Questionnaire Scores, and statistics analysis

Demographic, Clinical features and Questionnaires´ Scores				
		Total (N = 53)		
Female, n (%)		34 (64.2)		
Age, years *		45.6±13.1 (19.0-81.0)		
IgG replacement route, n (%) IVIG SCIG		 41 (77.4) 10 (18.9)		
Clinical manifestations, n (%) Infections in the preceding 3 months Autoimmunity/ Chronic diarrhea Splenomegaly/ Adenopathies Granulomatous disease/ Bronchiectasis Liver hyperplasia /Malignancy		 33 (62.3) 32 (60.4)/37(64.9) 38 (71.7)/19 (35.8) 29 (54.7)/37 (69.8) 5 (9.4)/6 (11.3)		
Questionnaires		**Scores**		
CVID-PT_QoL (0-100%) Global Emotional Functioning Gastrointestinal and Skin Symptoms Relational Functioning		 29.4 (16.5) 32.3 (17.2) 29.6 (20.6) 24.3 (16.09)		
SF-36 (0-100%) Physical Component Summary Mental Component Summary		 50.0 (18.5) 60.2 (3.4)		
HADS A (0-21points)		6.7 (3.4)		
HADS D (0-21points)		4.7 (3.8)		
CVID-PT_QoL, SF 36 and HADS according to route of replacement therapy				
Characteristics		**IVIG N= 41**	**SCIG N=10**	***P - value* IVIG *vs* SCIG**
Female, n (%)		**27 (65.9)**	**6 (60)**	**< .0001**
CVID-PT_QoL (0-100%) Global Emotional Functioning Gastrointestinal and Skin Symptoms Relational Functioning		 **32.2 (16.7)** **35.6 (16.9)** 32.2 (21.4) 26.0 (16.3)	 **21.7 (12.8)** **23.6 (14.4)** 21.3 (14.4) 20.5 (15.3)	 **.042** **.037** ns ns
SF-36 (0-100%) Physical Component Summary Mental Component Summary		 **46.2 (18.1)** **56.4 (19.0)**	 **60.8 (14.7)** **72.4 (14.5)**	 **.016** **.009**
HADS A (0-21points)		**7.3 (3.4)**	**4.9 (2.7)**	**.030**
HADS D (0-21points)		5.3 (3.9)	3.2 (3.0)	ns
Correlation	**CVID-PT_ QoL Global**	**Emotional Functioning**	**Gastrointestinal and Skin Symptoms**	**Relational Functioning**
SF-36 PCS	-.751**	-.739**	-.502**	-.687**
SF-36 MCS	-.828**	-.790**	-.660**	-.755**
HADS A	.723**	.696**	.636**	.590**
HADS D	.693**	.613**	.569**	.658**

CVID – Common Variable Immunodeficiency; IVIG – Intravenous Immunoglobulin; SCIG – Subcutaneous Immunoglobulin. Scores expressed as percentages were presented as mean (SD). ns – not statically significant. Mann-Whitney test (GraphPad Prism software); PCS – Physical Component Summary; MCS – Mental Component Summary; *P < .01 ; **P < .001. Test Spearman correlation (GraphPad Prism software)

The CVID-PT_QoL questionnaire scores are especially valuable to monitor CVID-specific health dimensions. Our data support the content validity and translatability of the *CVID-PT_QoL* questionnaire, as well as its implementation in clinical practice. We encourage future research with longitudinal data and a sizable study population to disentangle the reciprocal effects of mental health and disease severity on overall QoL outcomes.

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Ethics approval and consent to participate

This study complies with the Declaration of Helsinki and with the local Ethics Committee (Comissão de Ética do Centro Académico de Medicina de Lisboa).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflict of interest

The authors have no conflicts of interest to declare.

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