Received: 6 April 2022 | Accepted: 10 April 2022

DOI: 10.1111/jns.12494

RESEARCH REPORT

WILEY

Validation of the Italian version of the pediatric CMT quality of life outcome measure

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Abstract

The pediatric Charcot-Marie-Tooth (CMT) specific quality of life (QOL) outcome measure (pCMT-QOL) is a recently developed and validated patient-reported measure of health QOL for children with CMT. The aim of this study was to provide and validate an Italian version of the pCMT-QOL. The original English version was translated and adapted into Italian using standard procedures. pCMT-QOL was administered to patients genetically diagnosed with CMT, aged 8 to 18 years. A retest was given 2 weeks later to assess reliability in all patients. A total of 22 patients (median age 14 years, DS 2.5; M:F 1:1) affected with CMT (19 CMT1A, 2 CMT2A, 1 CMT2K) were assessed as part of their clinical visit. The Italian-pCMT-QOL demonstrate a high test-retest reliability. None of the patients experienced difficulty in completing the questionnaire, no further corrections were needed after administration in patients. The Italian-pCMT-QOL is a reliable, culturally adapted and comparable version of the original English pCMT-QOL. This questionnaire is expected to be valuable in monitoring disease progression and useful for future clinical trials in Italian-speaking children with CMT.

KEYWORDS
Charcot-Marie-Tooth disease, children, patient-reported outcome measures, quality of life, translation

1 | INTRODUCTION

Charcot-Marie-Tooth disease (CMT) is the most common inherited neuromuscular disorder, affecting approximately 1:2.500 subjects,[1] and exhibiting wide phenotypic and genetic heterogeneity.

Patients typically present with a slowly progressive motor and sensory neuropathy characterized by distal muscle atrophy and weakness, foot deformity, hypo-areflexia, and sensory disturbances. More than 90 distinct genes have been associated with CMT, involved in a number of different molecular pathomechanisms, ranging from protein synthesis and posttranslational processing, to intracellular trafficking, dysfunction of ion channels or mitochondria.[2,3]

The clinical impairment is frequently present since the pediatric age with variable levels of disability.[4]

Although no disease-modifying treatment has yet been identified, a number of promising compounds are currently under investigation

TABLE 1 Results of the pCMT-QoL (Italian) assessment

ID	Diagnosis	Sex	Age at evaluation (years)	Symptoms	Function	Social activities	Feeling	Cognition	Social skills	Physical composite domain score	Mental composite domain score	Total pCMT-QOL score
1	CMT1A	M	13	26.68	3.81	25.64	15.07	18.97	7.29	19.72	14.83	17.58
2	CMT1A	M	13	22.37	15.98	25.52	4.37	9.91	3.51	21.42	6.32	14.80
3	CMT1A	M	11	29.17	19.55	28.20	13.01	30.77	20.59	26.09	21.60	24.12
4	CMT1A	M	17	7.35	0.00	17.49	3.21	10.41	0.00	8.16	5.28	6.90
5	CMT2A	F	14	42.17	34.03	57.97	32.63	30.53	10.82	44.40	26.90	36.73
6	CMT2A	M	11	12.04	2.39	13.48	6.64	52.81	10.91	9.65	25.48	16.59
7	CMT1A	F	18	21.24	13.15	40.27	18.67	18.31	19.30	24.42	18.67	21.90
8	CMT2K	F	15	17.79	52.65	46.62	9.16	0.00	10.60	36.33	5.94	23.00
9	CMT1A	F	17	2.26	0.00	5.42	2.19	12.64	7.29	2.52	7.38	4.66
10	CMT1A	F	14	28.84	7.92	32.82	13.35	37.97	0.00	23.90	19.88	22.14
11	CMT1A	M	17	19.77	6.95	33.02	15.88	35.86	19.30	19.89	24.39	21.86
12	CMT1A	F	14	17.70	23.69	35.75	28.94	5.90	11.88	24.69	16.17	20.96
13	CMT1A	M	17	8.55	2.39	16.22	6.08	12.43	16.21	8.99	10.82	9.79
14	CMT1A	F	13	25.70	12.85	37.58	12.42	5.37	11.08	25.42	9.39	18.39
15	CMT1A	M	18	19.22	18.00	24.65	0.00	6.43	5.06	20.44	3.59	13.17
16	CMT1A	F	16	41.90	37.80	71.94	55.49	36.89	28.41	49.45	42.19	46.26
17	CMT1A	F	9	19.29	5.67	33.25	6.57	15.60	2.59	19.38	9.17	14.91
18	CMT1A	M	13	32.47	25.45	38.94	26.62	58.57	23.34	32.31	38.26	34.92
19	CMT1A	F	16	21.99	3.81	10.79	8.45	0.00	2.59	13.44	3.86	9.24
20	CMT1A	F	14	36.23	11.89	29.59	16.57	14.33	32.19	27.21	19.22	23.71
21	CMT1A	M	13	3.05	0.00	0.00	21.90	0.00	0.00	1.27	8.49	4.44
22	CMT1A	M	11	12.76	8.76	10.87	6.64	17.72	3.08	11.04	10.13	10.64

TABLE 2 Scores per Individual Domains, Composite Domains and Total pCMT-QoL

Domain	n Pts	Mean	SD	Minimum score in current study sample	Maximum score in current study sample
Symptoms	22	21.09	12.98	2.26	56.68
Function	22	15.00	13.81	0.00	52.65
Social Activities	22	27.45	18.07	0.00	71.94
Feeling	22	15.65	13.48	0.00	55.49
Cognition	22	19.23	15.69	0.00	63.19
Social Skills	22	11.53	9.08	0.00	32.19
Physical Composite Domain Score	22	21.17	13.20	1.27	54.94
Mental Composite Domain Score	22	16.10	10.59	2.46	42.19
Total pCMT-QOL Score	22	18.96	10.92	4.44	46.26

in preclinical and clinical research.[5] Particular interest has been directed towards pediatric trials, as signs and symptoms can progress throughout childhood, and early intervention before substantial axonal loss is more likely to be effective.[6] Therefore, specific outcome measures validated for pediatric CMT are needed to assess disease progression and response to therapy, including patient-reported outcome measures (PRO).[7]

Generic health-related quality of life (QOL) has been used in children with CMT in past years.[8,9]

Recently, Ramchandren and colleagues[10] developed and validated the pCMT-QOL, a disease-specific self-administered PRO measure for natural history studies and clinical trials in English-speaking children aged 8 to 18 years. It consists of 57 items divided into six domains significant for QOL in children with CMT (Symptoms, Function and Social Activities, Feelings, Cognition and Social Skills), grouped into two Composite domains, Physical and Social, respectively. Scores range from 0 to 100 where higher scores indicate greater disease severity.

The lack of an Italian version of this questionnaire limits its use among Italian-speaking individuals. Therefore, the aim of this study was to translate pCMT-QOL from English and validate the Italian version (I-pCMT-QOL).

2 | MATERIALS AND METHODS

We first contacted and obtained permission to use the instrument and perform the translation from the pCMT-QOL developers (SR, MS). A parallel reverse translation process was used as a quality assurance method.[11]

The questionnaire was translated and culturally adapted into Italian by two pediatric neurologists with experience with CMT and good English language proficiency (IM, EP). Subsequently, two additional neurologists experienced in CMT (DP, GP) reviewed both translations and developed a single provisional version as precisely as possible, which was then back-translated into English by a mother tongue certified translator who was blinded with respect to the original version. Next, the entire panel of experts (IM, EP, DP, PG) compared the translated version in English with the original version of the pCMT-QOL to confirm the accuracy and correspondence of the concepts, to reconcile any meaningful differences and to identify any potentially problematic or confounding factor. The formal process of translation produced the final version of the I-pCMT-QOL that was administered to a series of Italian children with CMT (8-18 years) as part of their clinical visit. This step assessed the questionnaire in real situations to ensure the understanding of the items and the instructions given. The second test administration (retest) was conducted remotely and sent back by email within a 2-week period. Finally, we assessed the validity and reliability in test-retest of the I-pCMT-QOL through intraclass correlation coefficient (ICC). ICC values of <0.40, 0.40 to 0.75 and >0.75 indicate poor, fair to good and excellent reproducibility, respectively.[12]

3 | RESULTS

The Italian version of the pCMT-QoL was administered at the Fondazione IRCCS Istituto Neurologico Carlo Besta in Milan by IM and EP to 22 children (11 females) genetically diagnosed with CMT (19 CMT1A, 2 CMT2A and 1 CMT2K) with a wide range of disease severity. Test-retest was performed in all patients. Table 1 summarizes anagraphic and genotypic data of the evaluated children and the results of all obtained scores. The average age of children was 14.27 years, SD 2.51 (range 9-18 years); the average total score of I-pCMT-QOL was 18.96 (SD 10.92; minimum score 4.44, maximum score 46.26).

Table 2 summarizes the mean of the Individual Domain scores, Physical Composite Domain and Mental Composite Domain scores.

The I-pCMT-QOL showed a high test-retest reliability (ICC 0.864, IC 95% 0.699-0.941).

No problems or difficulties were identified during the administration of the questionnaire, and the completion time (approximately 20 minutes) was suitable with clinical practice. Therefore, no further revisions were needed and the final version of the I-pCMT-QOL was achieved (Figure S1).

4 | DISCUSSION

In the last years, a number of potential treatments for CMT are under investigation, and the pediatric population might be of particular interest for early stage treatment. For this reason, the availability of meaningful and specific outcome measures, including pediatric patient-reported questionnaire, is a fundamental requirement. Moreover, in preparation for international trials, a proper translation and validation of those instruments in different languages would be needed.

The CMT Pediatric Scale (CMTPedS)[13] is currently used for measuring the severity of disability in children over 3 years old and has been widely translated.[14,15]

Recently, the pCMT-QOL, a disease-specific self-administered PRO measure for children aged 8 to 18 years, was generated for natural history studies and clinical trials for English-speaking patients with CMT. We translated and validated this tool into Italian through a translation and back-translation formal process. We administered the final version to 22 pediatric patients with CMT confirming high test-retest reliability. Patients reported not issues in completing the questionnaire.

The I-pCMT-QOL represents a culturally adapted, reliable and comparable version of the original pCMT-QoL. It is ready for use as part of clinical evaluations, monitoring disease progression and future clinical trials in Italian-speaking CMT children.

ACKNOWLEDGEMENTS

IM, FRD, AA, EP and DP are members of the European Reference Network for Neuromuscular Disorders (ERN-NMD).

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Moroni I, Danti FR, Pareyson D, et al. Validation of the Italian version of the pediatric CMT quality of life outcome measure. *J Peripher Nerv Syst*. 2022;27(2):127-130. doi:10.1111/jns.12494