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Tremor-related quality of life: A comparison of essential tremor vs. Parkinson's disease patients

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ABSTRACT

Background: Tremor-related quality of life is a multi-dimensional concept that reflects the physical, emotional and other health effects of tremor. Curiously, tremor-related quality of life has never been directly compared in patients with the two major tremor disorders, essential tremor (ET) and Parkinson's disease (PD). We performed a head-to-head comparison of ET with PD patients.
Methods: The Quality of Life in Essential Tremor (QUEST) questionnaire was administered to 103 ET and 103 matched PD patients enrolled in a clinical-epidemiological study in New York.
Results: The QUEST total score and QUEST physical subscore were higher in ET than PD patients (both $p < 0.05$). In relative terms, ET patients reported significantly more impairment than PD patients in multiple areas; PD patients reported more impairment than ET patients in one area (all $p \leq 0.02$). In absolute terms, tremor impacted on many aspects of quality of life in both diseases, including physical and psychosocial, and in one-third or more of PD patients, tremor sometimes, frequently or always interfered with numerous physical activities, including writing, using a typewriter/computer, fixing small things, dressing, eating, and holding reading material.
Conclusions: Tremor is a clinical entity that can have numerous effects on patients. While there were relative differences between the two major tremor disorders, ET and PD, in absolute terms, tremor impacted on several domains of quality of life, from physical to psychosocial, in a large proportion of ET and PD patients. Attempts to judge the efficacy of treatments for tremor, whether pharmacological or surgical, should consider its broad impact.

1. Introduction

Health-related quality of life (HRQoL) is a multi-dimensional concept that includes a number of distinct domains, which are related to physical, mental, emotional and social function. To gauge the effects of chronic illness on quality of life, clinical researchers have used a variety of HRQoL questionnaires.

Essential tremor (ET) is a chronic and progressive neurological disease, eventually impacting numerous aspects of daily function [1,2]. The Quality of Life in Essential Tremor (QUEST) questionnaire is a specific measure of tremor-related quality of life [3,4], and its recent introduction has given rise to a growing literature on tremor-related quality of life in ET. Although informative, available studies have a number of limitations, which include the enrollment of surgical patients with significant and disabling tremor whose experiences cannot be extrapolated to most patients with ET [5], the enrollment of very young patients whose age is not typical of ET patients in developed countries [6], and small samples enrolled in specific therapeutic settings (e.g., clinical trials) [7]. QUEST data from several countries, including Spain [3] and India [6], have been published; by contrast, data from patients in the United States are limited [8]. Most important is that, aside from one study in India [6], data on the >30 individual items that richly comprise the QUEST have not been presented in any published study.

Nearly all of the items on the QUEST relate both specifically and explicitly to tremor and its effects on perceived health. Curiously though, the instrument has not been applied to patients with Parkinson's disease (PD), despite the fact that (1) tremor is a hallmark feature of PD, (2) tremor, whether rest, postural or kinetic, occurs in the large majority of PD patients at some point during the illness,

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(3) and action tremor has been reported in >90% of PD patients [9]. One important caveat; however, is that the psychometric properties of the QUEST have not been assessed in a group of PD patients; hence, assessing these attributes is an important step.

Furthermore, tremor-related quality of life has not been directly compared using the same instrument in the two major tremor disorders, ET and PD. Hence, a head to head comparison has yet to be performed.

The goals of this study were to (1) use the QUEST to present a fine-grained view of tremor-related quality of life in a cohort of patients with ET enrolled in a clinical-epidemiological study in the United States, (2) assess the psychometric properties of the QUEST in PD patients, and (3) directly compare tremor-related quality of life in patients with ET vs. PD.

2. Methods

2.1. Participants

Participants were enrolled in a clinical-epidemiological study of movement disorders at the Neurological Institute, Columbia University Medical Center (CUMC) (2009–2014) [10,11]. The study assessed the role of environmental toxins in disease etiology; it also assessed a wide range of clinical features. ET and PD patients seen in the most recent 5 years were identified from a computerized billing database at the Center for Parkinson's Disease and Other Movement Disorders at the Institute. Each patient had received a diagnosis of ET or PD from their treating neurologist at the Institute. One of the authors (E.D.L.) reviewed the office records of identified patients; those with diagnoses of or physical signs consistent with other movement disorders were excluded. During the review, the most recent Hoehn & Yahr score [12] and daily dose (mg) of levodopa were recorded for PD patients.

The CUMC Internal Review Board approved study procedures. Signed informed consent was obtained upon enrollment.

2.2. Study evaluation

During the in-person assessment, a trained research assistant administered a series of structured questionnaires, which elicited data on (1) demographic variables, (2) general medical health (Cumulative Illness Rating Scale score [13] (range = 0–42 [maximum]), total number of prescription medications), (3) disease severity or stage (e.g., duration of symptoms, taking medication to treat tremor [yes vs. no]), and (4) additional variables of interest (e.g., age of tremor onset, family history [first- or second-degree relative] of ET, family history of PD).

The Center for Epidemiological Studies Depression Scale (CESD-10) was administered – a self-report ten-item screening questionnaire for depressive symptoms (range = 0–30 [greater depressive symptoms]) [14]. The Essential Tremor Embarrassment Assessment, a 14-item assessment of tremor-related embarrassment (range = 0–70 [maximal embarrassment]) [15] was administered to ET patients.

The QUEST was administered [4] to ET and PD patients. In this questionnaire, 30 items are rated on a five-point scale (0–4), corresponding to the frequency (never, rarely, sometimes, frequently, always) with which tremor is perceived to currently impact a function or to be associated with various feelings or attitudes [4,8]. Items are grouped into five domains: physical (n = 9, e.g., tremor interferes with eating), psychosocial (n = 9, e.g., tremor interferes with relationships with others), communication (n = 3, e.g., tremor interferes with ability to communicate), hobbies/leisure (n = 3, e.g., tremor caused the individual to quit hobbies), and work/finance (n = 6 items) [4]. There are 6 additional items in which tremor is rated in the head, voice and each limb (for each, score 0–4), corresponding to the severity of tremor (none, mild, moderate, marked, severe). Four items from the work/finance domain did not apply to the vast majority of our patients, who were elderly, so that in our analyses of the psychometric attributes of QUEST in PD, we used a 26 item version of QUEST that included only the two relevant work/finance items (tremor resulted in early retirement, tremor lead to financial problems/concerns).The psychometric attributes of QUEST in ET patients have been assessed and most are satisfactory [3,4]. The psychometric attributes of QUEST have not been assessed in PD, and this was an aim of this study.

A videotaped neurological examination was performed on ET patients. This included one test for postural tremor and five for kinetic tremor (e.g., pouring, drinking) performed with each arm (12 tests total). A neurologist specializing in movement disorders (E.D.L.) used a reliable [16] and valid [17] clinical rating scale, the Washington Heights-Inwood Genetic Study of ET (WHIGET) tremor rating scale, to rate postural and kinetic tremor during each test: (0–3). These ratings resulted in a total tremor score (range = 0–36) [18].

2.3. Diagnoses

ET diagnoses were re-confirmed (E.D.L.) using the videotaped neurological examination and WHIGET diagnostic criteria (moderate or greater amplitude kinetic tremor [tremor rating ≥2] during three or more tests or a head tremor, in the absence of PD, dystonia or another cause) [19]. The WHIGET diagnostic criteria for ET were developed for a population-based genetic study and, based on data from approximately 2000 normals (non-diseased controls), these criteria carefully indicate the specific examination maneuvers during which tremor should be present and the severity of tremor that should be evident during these maneuvers. These criteria have been shown to be reliable [16] and valid [18], and are used routinely in Dr. Louis' epidemiological studies of ET [20,21] and those of other tremor investigators in the US and internationally [22,23]. The diagnosis of PD was confirmed (E.D.L.) using published diagnostic criteria [24].

2.4. Final subject selection

QUEST data were available on all 103 PD patients. These were compared to data on 103 ET patients who were frequency-matched to the PD patients by age and gender.

2.5. Statistical analyses

Data were analyzed in SPSS (Version 21). Demographic and clinical characteristics of ET and PD patients were compared using chi-square tests, Student's t tests, or Mann–Whitney tests (if the variable was not normally distributed) (Table 1).

We evaluated a number of psychometric attributes of the QUEST total score and each of five subscores: (1) *acceptability* (missing data [standard acceptable value <5%], difference between mean and median [standard ≤10% of the maximum possible score], and floor and ceiling effects [maximum acceptable limit 15%]), and (2) *reliability* (internal consistency determined by Cronbach's alpha coefficient [standard value ≥0.70], item–item correlation coefficients using Spearman's rho (values between 0.30 and 0.70 = moderate and values >0.70 = high), and reproducibility [test-retest reliability] using the intraclass correlation coefficient (one-way random-effects model, single measure)[threshold value for groups ≥0.70]) [3]. These analyses (Table 2) were restricted to the 88 PD patients who reported tremor.

Rather than selecting only those patients who self-reported tremor, our goal in assessing quality of life was to obtain a global (i.e., broad and all-encompassing) view of PD in all-comers (i.e., all patients who were encountered). Furthermore, in these and prior analyses, we have found that even among patients who self-report no tremor, there can be mild or intermittent tremor, with associated self-reported changes in tremor-related quality of life on detailed questioning, further justifying our reluctance to attempt to selectively remove some PD patients from the analyses of tremor-related quality of life. Nonetheless, in one analysis, we also reported results after having removed a small number of PD cases who did not report tremor.

QUEST data were compared in ET vs. PD patients either using Mann–Whitney tests (for QUEST total score and each of five QUEST subscores) or a linear-by-linear test of association (for ordinal data on each of the QUEST's 36 self-assessment items) (Table 3). We assessed correlations between the QUEST total score and QUEST physical subscore and several measures of disease severity or duration both in ET and PD patients (Spearman's rho).

3. Results

The 103 ET and 103 PD patients were similar in age, gender, race and education (Table 1). The two groups did not differ with respect to Cumulative Illness Rating Scale scores or total number of prescription medications used. As expected, the age of onset was younger and tremor duration was longer in ET than PD, and the two groups differed with respect to the proportion with a family history of ET or PD (Table 1). Interestingly, a marginally higher percentage of PD than ET patients was taking medication to treat tremor (Table 1).

We assessed a number of psychometric attributes of the QUEST total score and each subscore. In terms of acceptability, missing data accounted for <5% of data and the difference between the mean and median value was less than 10% of the maximum possible score for the total QUEST score and three of five QUEST subscores (Table 2). Floor effects were <15% for the total score and two of five subscores. Ceiling effects were very low (≤4.7% for the total score and each subscore). Cronbach's alpha coefficient was uniformly higher than 0.70. Item–item correlation coefficients had a broad range (Table 2); most of these fell in the 0.3–0.7 (moderate) range (2/3 for communication subscore, 1/1 for work-finance subscore, 3/3 for the hobbies/leisure subscore, 34/36 for the physical aspects subscore, and 29/36 for the psychosocial aspects subscore). The intraclass correlation coefficient was in the 0.36–0.66 range (Table 2).