Clinical Rating Scales for Urinary Symptoms in Parkinson Disease: Critique and Recommendations.

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ABSTRACT

Background: The prevalence of lower urinary tract symptoms (LUTS) is high in Parkinson`s disease (PD). These problems negatively affect quality of life and include both storage and voiding problems. The International Parkinson and Movement Disorder Society established a Task Force to review clinical rating scales/questionnaires for the assessment of urinary symptoms in PD.
Methods: According to pre-specified criteria, these scales/questionnaires were classified as "Recommended", "Recommended with caveats" when clinimetric properties were satisfactory for Recommended status but had not been assessed specifically in PD, "Suggested" or "Listed". These assessments were applied to rate scales as screening tools for the diagnosis of LUTS and for the rating of symptom severity.
Results: Among scales that included LUTS but focuses on overall autonomic or non-motor symptoms in PD, no scale reached the clinimetric rigor to be designated as Recommended or Recommended with caveats, but some were Suggested for either diagnostic screening tools or severity measures. Among primary urological scales, most are well validated in urological setting, but none was validated specifically in PD. DAN-PSS (Danish PSS), ICIQ (International Consultation for Incontinence Questionnaire)-MLUTS (Male Lower Urinary Tract Symptoms), OABq, OABq-SF (ICIQ-OABqol), OAB-V8 (as screening tool) and OABSS (OAB Symptom Score) met criteria for "Recommended with caveats".
Conclusion: The Task Force does not recommend the development of a new scale. However, all above-mentioned questionnaires need to be studied further and specifically validated in PD.

Introduction

Urinary symptoms are common and often complex in Parkinson Disease (PD), adversely affecting quality of life (QoL) (1). The etiology of lower urinary tract symptoms (LUTS) is mediated by complex mechanisms (involving central brain areas, somatic and autonomic nerves) that are not fully understood. The most frequent bladder symptoms are due to disorders of storage, and include nocturia, frequency, urgency, urge incontinence and voiding dysfunction. Voiding problems can also occur with difficulty in the initiation of micturition and a poor stream (1-4). Moreover, mechanical intercurrent pathologies can be observed in PD as BPH (benign prostatic hyperplasia) or genital prolapse in women, complicating evaluation and treatment of urinary disorders.

The timing of onset and the nature of bladder symptoms may help to differentiate among the parkinsonian syndromes (5-7). Their prevalence in PD differs according to the studies, depending on the evaluation tools and the populations studied; it has been reported as being between 27-39% (2, 8) or up to 54% for urgency and 63% for night time frequency (3). Yeo et al (9) report storage and voiding symptoms in 57-83% and 17-27% PD patients respectively.

Although, there are "gold standard methods" for assessing LUTS in the laboratory (as urodynamic assessment), validated questionnaires and clinical rating scales are necessary to easily detect and characterize LUTS in clinical practice.

Therefore the Movement Disorder Society established a task force to review clinical rating scales for the assessment of urinary symptoms in PD.

Methods

Administrative Organization and Critique Process

The committee who composed the Task Force included eight neurologists and urologists, a statistician with clinimetric expertise and an expert in questionnaire design and validation from North America and Europe. The committee members assessed the scales' previous use, examined their clinimetric properties, and evaluated their clinical utility.

Literature Search Strategy

A systematic search was conducted using PubMed and Medline entering the combined search terms "bladder" or urinary" or "LUTS" or "nocturia" or "incontinence" and "Parkinson" in the English literature. Papers were retrieved, examined and references were searched for rating scales or questionnaires on bladder dysfunction. Only published or *in press* peer-reviewed papers until April 2017 were considered for analysis.

Selection of Scales and Questionnaires

Scales and questionnaires previously used in clinical studies with PD patients were searched for further evaluation. If the scales/questionnaires applied in PD patients were not validated in this population, validation data from other populations were

considered. General scales/questionnaires, which included these urinary symptoms, were also considered for analysis.

Evaluation of Scales and Questionnaires

Clinimetric properties were analyzed to criteria detailed in a previous report (10). According to the MDS task force criteria, each scale was rated as following: A scale was classified "Recommended" if it has been:1) applied to PD populations; and 2) used in studies beyond the group that developed the scale, and 3) studied clinimetrically and found reliable, valid, and sensitive to changes. The clinimetric criteria could be met by documentation of the scale's sound properties in conditions other than PD, but scales validated in PD itself were rated at a higher level. A scale was "Recommended with caveats" when a well-validated scale has not been specifically tested for clinimetric properties in PD and needs further validation in this population. A scale was considered "Suggested" if it has been applied to PD populations, but only one of the other criteria applies. A scale was considered "Listed" if only applied to PD populations.
Some of these scales provide information on the severity and/or frequency of the urinary symptoms whereas others can be considered as screening tools since they only look for these symptoms in a general way and/or without scoring their severity and/or frequency.

Results

Three different kinds of scales or questionnaires to assess urinary dysfunction in PD were found. First, ratings of urinary dysfunction are part of larger and more general scales designed to assess autonomic or non-motor symptoms in PD patients or, second, are contained within larger and generic autonomic function scales that have also been used in PD patients (Table 1). In these two scenarios clinimetrics have been performed on the full scale. To our knowledge there are no data showing that the items or factors or subcomponents relative to urinary function in these scales/questionnaires have clinimetric strengths. General clinimetric properties and time-to-administer of each of them are summarized in Table 2.
The third category of scales or questionnaires are focused on urinary symptoms, usually designed for primary urological disorders and then applied to PD patients. Clinimetric properties and time-to-administer of each of these scales are summarized in Table 3.

Some sleep questionnaires can be used to assess nocturia and nocturnal incontinence such as the Parkinson's Disease Sleep Scale. However these scales are mainly focused on sleep disturbances and not on urological symptoms and were not considered for further analysis.

Detailed clinimetric properties of "Recommended with caveats" and "Suggested" scales/questionnaires are given in supplemental material.

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General scales or questionnaires designed to assess autonomic or non-motor symptoms in PD or in general medical conditions

A total of 9 scales or questionnaires designed to assess non-motor or autonomic symptoms in PD patients were identified and screened for full review (3, 11-18) (Table 1).

Severity scales

*SCales for Outcomes in PArkinson's disease – AUTonomic dysfunction (SCOPA-AUT)

Description and clinical use

The SCale for Outcomes in PArkinson's disease - AUTonomic dysfunction (SCOPA-AUT) is a self-administered questionnaire consisting of 25 items designed to evaluate the presence and frequency of autonomic symptoms (11). There are six domains including different items and each item is scored 0-3 with higher being worse (0=never) to 3=often). The urinary domain includes 6 questions related to the following symptoms: urgency, urinary incontinence, incomplete emptying, weak stream of urine, frequency and nocturia. An additional response option may serve to indicate whether subjects used a catheter or not. Verbaan et al (19) used the SCOPA-AUT in a large cohort of patients with PD (420 patients), and compared the scores to 150 control subjects. 37.4 % of the patients had urinary symptoms.

Key evaluation criteria

The SCOPA-AUT was specifically developed to be applied to PD patients and has been used by other groups (20,21). The SCOPA-AUT is a reliable and easily self-administered questionnaire for assessing presence and severity of autonomic symptoms in PD patients. The 6 urinary items assess both filling and voiding phases. Independent validations of this scale have been conducted (22, 23) and found the SCOPA-AUT an acceptable, consistent, reliable and valid scale. However responsiveness has not been evaluated to determine the sensitivity of the complete scale to detect change and to our knowledge, the SCOPA-AUT urinary sub-score has never been validated separately.

Conclusion

The SCOPA-AUT is classified as "Suggested" as it has only been shown to assess severity of urinary symptoms as a part of autonomic symptoms and there are insufficient clinimetric data for the urinary subdomain.

*Non-Motor Symptoms Scale (NMSS)

Description and clinical use

The NMSS was developed to provide a method to quantify non-motor symptoms as evaluated in the NMS Quest (screening tool) (12). The NMSS is rated by the health professionals. The NMSS is divided into nine major domains containing 30 questions, including 3 urinary items (Urgency, Frequency, Nocturia). The NMSS reflects the questions flagged in the NMS Quest. Item scoring is obtained multiplying the severity score (ranging from 0=”none” to 3=”severe”) and the frequency score (from 1=”rarely” to 4=”very frequent”).

Key Evaluation criteria

The NMSS (rater-based) has been developed to quantify NMS. The scale can capture severe but relatively infrequent non-motor symptoms and those less severe but persistent in PD. The full scale has been clinimetrically validated thoroughly, showing good convergent and discriminative validity, and satisfactory test-retest reliability (12). A good responsiveness to changes has been reported in clinical trials (24-26). It has been used by others than the original developers (24, 26). Urinary assessment includes only 3 symptoms. Clinimetric properties for urinary symptoms have not been evaluated separately.

Conclusion

The NMSS meets the designation of “Suggested” as it has only been shown to successfully assess severity of some bladder symptoms as a part of non-motor symptoms and there is no intended focus on urological features.

***Questionnaire on pelvic organ dysfunction in PD patients**

Description and clinical use

This questionnaire has been designed to assess pelvic organ dysfunction in PD including bladder, bowel and genital related items (respectively 9, 4 and 3 (women) to 5 (men)); each item can be given a quantitative score (4 levels for each item). It includes questions about the filling phase as well as the voiding phase.

Key evaluation criteria

This study by Sakakibara et al (3) assesses a range of bladder disorders which may occur in PD. Answers are quantitative, which would seem to be essential if the scale is to be used for research purposes rather than simply screening. The same group used this questionnaire to help to distinguish PD and MSA-P (27).
However the clinimetric properties of this questionnaire have not been evaluated.

Conclusion

Despite its interest this questionnaire meets the designation of “Listed ”as it has not been validated and used by other groups yet.

*** Questionnaire on« autonomic dysfunction in PD»**

Description and clinical use
This questionnaire proposed by Siddiqui et al. (17) includes different autonomic domains (cardio-vascular (CV),Gastro-Intestinal (GI), sudomotor, sexual and bladder) with 7 urinary symptoms (hesitancy, urgency, incomplete voiding, weak stream, frequency, nocturia, incontinence). The severity of symptoms was graded on a 0-4 score.

Key evaluation criteria
The study reporting the use of the instrument is a cross-sectional study. The findings confirm that autonomic dysfunction occurs in PD patients more than in controls (no PD) and with greater severity. There were limitations to this study: the sample size was small resulting in possible Type II errors. Validity and test-retest reliability were not examined. Time to administer was not discussed.

Conclusion
This questionnaire meets the designation of "Listed" as it has not been validated and used by other groups yet.

***Questionnaire on «bladder and autonomic dysfunction in PD »**

Description and clinical use
This self -report questionnaire proposed by Hobson et al. (18) has been designed to estimate the prevalence of bladder and autonomic symptoms in a sample of PD patients and a healthy elderly control group–. Nine items are related to bladder dysfunction related to filling and voiding phases and assess the following symptoms: frequency, urgency, urinary incontinence, incomplete emptying, weak stream of urine, burning sensation and nocturia. Two additional items assess the QoL. Each symptom was scored on a 1–5 scale, with increasing values indicating greater symptom severity.

Key evaluation criteria
This questionnaire, based on a previous (non-validated) scale used by Berrios et al. (1995) is mainly focused on bladder symptoms. Nine items are related to bladder dysfunction and 2 items to sexual matters. This questionnaire has not been validated.

Conclusion
This questionnaire meets the designation of "Listed" as it has not been validated and used by other groups yet.

Screening tools

***Self-completed Non Motor Symptoms: Questionnaire for Parkinson's disease (NMS Quest)**

Description and clinical use*:*

The NMS Quest (NMS-Q) is a self-completed questionnaire, consisting of 30 items used to evaluate global non-motor function including different autonomic domains (2 for urinary) scoring as "yes" or "no" (14). Only 2 questions are related to urinary symptoms (urgency and nocturia). This is the first validated instrument of this type for PD patients. It is a screening tool. Different authors used the NMS-Quest to assess NMS and to investigate which factors influence them; urinary symptoms were among the most frequent NMS (28, 29).

Key evaluation criteria

The full NMS Quest is the first validated evaluation tool for assessing non-motor symptoms in PD, evaluated in multiple centers internationally, with good sensitivity and high specificity (30, 31). It is easy to score.

Because it is not a rating scale, this questionnaire can only be used for the screening of urinary symptoms (2 items) as a part of non-motor symptoms and cannot be used to assess their severity. There are no data showing that the items relating to urinary function have clinimetric strengths.

Conclusion

The NMS Quest meets the designation of "Suggested" as a screening tool for urinary symptoms as it has only been tested for urinary symptoms as a part of non-motor symptoms.

*** Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I**

Description and clinical use

One item deals with urinary problems in the new version MDS-UPDRS This item is assessed with the 0 to 4 rating system and was not captured in the previous UPDRS version (frequency, urgency, and incontinence as the most severe stage). The question was developed as a screening tool.

Key evaluation criteria

The full scale MDS-UPDRS meets criteria 1 and 2 as this scale has been validated in PD patients and recently been used by several groups. Expanded and independent validations in other languages have been published (32, 33).

Recent studies undertaken to determine the validity of MDS-UPDRS Part I showed that the Part I total score had a strong relationship with validated scales for the NMS (34, 35). However, the scale has not been separately and specifically validated in the realm of the urinary symptoms. The item on urinary symptoms had a moderate and significant correlation (r=0.55) with the SCOPA-AUT urinary sub-score.

Conclusion

The MDS-UPDRS can be classified as "Suggested" as it has only been shown to screen for urinary symptoms as a part of non-motor experiences of daily living and clinimetric properties for the single urinary question are not sufficient.

***Questionnaire on « symptoms of autonomic failure in PD »**

Description and clinical use
Developed in 2004 by a German centre in Freiburg (16), the questionnaire considers symptoms of autonomic failure in PD and their impact on daily life. In 5 short questions and 4-7 sub-items each, the main domains of autonomic failure are represented. In case of urinary symptoms, the patient is asked to answer to 4 sub-items related to frequency, incontinence, symptoms duration and QoL.

Key evaluation criteria
This tool discriminated well between PD patients and controls. It is short and easily administered. However the questionnaire is not validated in English and there are no clinimetric data for the urinary subdomain. It has not been used by other groups yet

Conclusion
This questionnaire meets the designation of "Listed" as it has not been validated and used by other groups yet.

General scales or questionnaires designed to assess autonomic symptoms in general medical conditions

Only one scale designed to assess autonomic symptoms in general conditions has been used in PD.

*** COMPosite Autonomic Symptom Score (COMPASS)**

Description and clinical use
Developed in 1999, the COMPASS is a general autonomic scale; it comprises 73 questions assessing 9 domains of autonomic symptoms including 3 questions for urinary symptoms. It has been used in a prospective study on MSA and PD patients with a large subset of PD patients with autonomic failure (25%) (36, 37).The same team recently developed a new scale the COMPASS 31, a refined, internally consistent, and abbreviated quantitative measure of autonomic symptoms based on the original ASP (Autonomic Symptom Profile) and COMPASS (38). The urinary items look for incontinence, difficulties to empty the bladder and incomplete bladder emptying. This revised scale has not been used in PD patients yet.

Key evaluation criteria
This questionnaire is thorough for assessing autonomic symptoms. It has to be evaluated more thoroughly in PD and seems too complex and extensive (73 items) for routine clinical purpose. Neither this questionnaire nor the COMPASS 31 assess frequent symptoms in PD such as urgency and nocturia. The only established clinimetric

properties of the full scale appear to be content validity and construct validity. There are no data showing clinimetric properties for the urinary domain. Validation of COMPASS and COMPASS31 is lacking in PD cohorts to date. This scale has not been used by other groups in PD patients.

Conclusion

Due to limited clinimetric validation and its use by only one group in PD, the COMPASS can be classified as "Listed" for the assessment of severity of urinary symptoms as a part of autonomic symptoms.

Generic clinical scales to assess bladder function in urological disorders and applied to PD

A total of 8 scales or questionnaires initially designed to assess various urological disorders and used in PD were identified and screened for full review. All these scales have been designed to assess the presence and severity of urinary symptoms.

*** International Prostate Symptom Score (IPSS)**

Description and clinical use

The validated American Urological Association (AUA) Symptom Index for BPH (39) together with an additional item on QoL was then named the International Prostate Symptom Score (IPSS) (40). The IPSS comprises seven questions (on incomplete emptying, frequent urination, intermittency, urgency, weak stream, straining to start, nocturia) that measure symptom frequency and severity, including an additional item measuring their impact on QoL. Each of the 7 symptom items has a response scale with six choices, scored from 0 to 5. Each respondent's IPSS yielded a value corresponding to the following severity ratings: 0, no LUTS; ≥1 but <8, mild LUTS; ≥8 but <19, moderate LUTS; ≥19, severe LUTS.

The IPSS has been used both in men and women for patients with neurological diseases; several teams used it in PD patients (2, 4, 9, 41, 42) including in advanced stage (43) and after Deep Brain Stimulation or rTMS (44-45).

Key evaluation criteria

The IPSS has become a commonly used instrument in multicentre, international clinical trials and has been translated into at least ten different languages (46-48). The instrument has been thoroughly validated and has an excellent internal consistency, good test-retest reliability, and good sensitivity and specificity (39, 40, 46-48,). This index provides a useful standard evaluation that could be used alongside others measures. The IPSS has been used both in men and women (49) and in patients with PD.

However, it was not designed for PD, was not enough sensitive to change in PD and would not provide items for assessment of some key problems encountered in PD like incontinence.

Conclusion
The IPSS meets the designation of "Suggested " for the assessment of severity of urinary symptoms, since this questionnaire has not been specifically validated in PD patients and is not enough sensitive to change.

*** Danish Prostatic Symptom Score (DAN-PSS)**

Description and clinical use
The DAN-PSS has been developed to implement a weighting of the symptoms by the patients based on the QoL (50, 51). It consists of 12 questions with integrated bother scores related to LUTS in 2 weeks prior to response. Compared to the IPSS, each symptom is both quantified and qualified by determining both a symptom score and a bother score. It is more sensitive to LUTS than the IPSS (52). The DAN-PSS has been used both in male and female patients (53,) and in PD, combined with IPSS (4, 43, 44). Another advantage of DAN-PSS compared to IPSS is the questions regarding incontinence.

Key evaluation criteria
The DAN-PSS is validated and has been used in several studies. It is a useful tool in describing the symptom severity in BPH. It is brief. It was designed for use in men only; however it has also been used in women even if it would require further validation in this population. It is reliable and has a strong discriminant and construct validity. The internal consistency of the instrument is also strong. It is sensitive to clinically change as shown in many intervention trials (51, 52, 53). A recent Turkish study showed that the Turkish version of this questionnaire was an internally consistent, reliable, and valid scale to assess frequency and severity of LUTS in PD in both sexes (54).

Conclusion
The DAN-PSS meets the designation of "Recommended with caveats" for the assessment of severity of urinary symptoms. Despite one limited validation study of the Turkish version in PD population, this questionnaire has to be evaluated more thoroughly in PD patients.

*** The International Consultation for Incontinence Questionnaire (ICIQ)-MLUTS**

Description and clinical use
The ICIQ-Male LUTS and ICIQ-Female LUTS have been validated and translated into many different languages with the aim of capturing symptomatology of the male and female LUTS, respectively (55,56); they are available on request (http://www.iciq.net). However, only the ICIQ-MLUTS and some specific modules have been used in PD patients.
The ICIQ-MLUTS (formerly the International Continence Society Male Short Form questionnaire (ICSmale SF)) (57, 58) was initially designed to assess LUTS and their

impact on the lives of men with benign prostatic disease. It consists of 13 questions to assess voiding dysfunction, urgency, incontinence, frequency, nocturia (+one additional question on the QoL in the ICS male SF). Using this questionnaire in PD patients both male and female, Sammour et al. (59) found that 57.2% of the PD patients (n=110 – 84 men) were symptomatic and that the voiding dysfunction was predicted by the PD disease severity and affected men and women alike. This questionnaire was recently used to assess the effects of transcutaneous tibial nerve stimulation on urinary disorders of PD (60).

Key evaluation criteria

The ICIQ-MLUTS questionnaire has been validated in patients for evaluating LUTS in research and clinical practice. –This questionnaire focusses on storage and voiding dysfunction in addition to incontinence. Studies showed that it was reliable and showed good construct validity and internal consistency. The reliability of most items was excellent (57, 58, 61). It was also sensitive to change following intervention (57, 58, 60). Validation has been done mainly in populations other than PD, but it has been used in several studies in PD, both in male and female patients.

Conclusion

The ICIQ-MLUTS meets the criteria of "Recommended with caveats" since further validation in PD is required for the assessment of severity of urinary symptoms

***The Over Activity of the Bladder Questionnaire (OAB-q)**

Description and clinical use

Several versions of this questionnaire have been designed to assess o~~O~~veractive bladder and the related QoL. The OAB-q is a 33-item module, specifically designed to assess the impact of OAB symptoms on QoL (62, 63). The OAB-q consists of a Symptom Bother scale and four QoL subscales (Coping, Concern, Sleep, and Social Interaction). All scale scores are transformed to a 0- to 100-point scale with higher Symptom Bother scores indicating greater symptom severity and lower QoL subscale scores indicating greater impact.

This instrument has been simplified in a short form (**OABq-SF**): The 8-item symptom bother scale of the OAB-q was reduced to 6 items, and the 25-item HRQoL scale of the OAB-q was reduced to 13 items (64). It has been adopted by the ICIQ committee as the questionnaire module for OAB (ICIQ-OABqol-Over Active Bladder QoL). This module is considered as a brief and robust tool to assess the impact of symptoms of OAB on QoL and outcome of treatment.

A simplest version also exists: the **OAB-V8** which is a patient self-administration screening tool. The eight item OAB-q addresses both the frequency and bother of frequency, urgency, nocturia, and incontinence symptoms (65).

Since in PD the urinary dysfunction manifests primarily with symptoms of OAB, several studies have evaluated them in PD using the OAB-q (54, 66, 67), the OABq-SF (60, 63)

and the OAB V8 (60, 69) to study the association of bladder dysfunction with other symptoms or to investigate the effects of treatment on urinary symptoms.

Key evaluation criteria

Both the OAB-q and the OAB-q SF (ICQ-OABqol) have demonstrated good internal consistency, test-retest reliability, construct validity, and responsiveness (62, 64). The OAB V8 demonstrated a good sensitivity and specificity to screen patients with bothersome OAB symptoms (65).

These 3 scales have been validated in patients with OAB and used in PD patients. They have been translated in several languages (69).

Conclusion

The OAB-q, the OAB-q SF and the OAB-V8 meet the designation of "Recommended with caveats " for the assessment of severity of OAB symptoms since further validation in PD is required. The OAB-V8 is considered as a screening tool.

*** Overactive Bladder Symptom Score (OABSS)**

Description and clinical use

The Overactive Bladder Symptom Score (OABSS) is a validated questionnaire designed to quantify symptom severity for four symptoms of daytime frequency, night-time frequency, urgency and urgency incontinence, based on the total score ranging from 0 to 15 points (70, 71). Daytime frequency is scored on a 3-point scale (0–2), night-time frequency on a 4-point scale (0–3), urgency on a 6-point scale (0–5), and urgency incontinence on a 6-point scale (0–5). A total of 3–5 was defined as ''mild'' in severity, a total score of 6–11 as ''moderate,'' and a total score of above 12 as ''severe.'' A score of 1 was defined as ''presence of symptom'' in each question. This questionnaire initially developed in Japan has been translated and validated in English (71, 72). It has been used in different populations suffering from symptoms of OAB, including for studying treatment effects. Several investigators used it in PD population (73-75).

Key evaluation criteria

Data showed that the OABSS had a good content and construct validity; the internal consistency was also satisfactory. It is a questionnaire, reliable and sensitive to drugs (70, 72, 76). It was used beyond the group that developed the scale. At least three studies reported its use in PD patients.

Conclusion

The OABSS meets the designation of "Recommended with caveats "for the assessment of severity of OAB symptoms since further validation in PD is required.

*** Urogenital Distress Inventory (UDI) – Short form**

Description and clinical use

The original urogenital distress inventory (UDI) was developed to assess the degree to which symptoms associated with incontinence are troubling (77). The UDI consists of 19 items comprising three domains: symptoms related to stress urinary incontinence, detrusor overactivity, and bladder obstruction.

A short form (SF) (6 items) of the UDI has been developed (78) to easily assess symptom distress of urinary incontinence and related conditions for women. This short form has been used once in PD by Lemack et al (79). ~~Women with PD had more urinary symptoms than non-age-matched volunteers, but less than women presenting for LUTS~~. Since age matched control UDI-6 data were not available, results were difficult to interpret.

Key evaluation criteria

Data showed that the UDI was reliable, valid and sensitive to change (79, 80). The short form correlated very strongly with the long form of the UDI questionnaire. This questionnaire is administered very quickly. However some clinimetric properties such as the internal consistency have not been evaluated on this Short Form. This questionnaire has been translated in several languages. Validation studies of both forms were conducted in a urology setting, and validated only in women. Only the UDI short form has been used in a female PD population without showing clear results.

Conclusion

The UDI short form has been validated and used by several groups. However this questionnaire was used only once in PD patients without clear results and therefore meets the designation of "Listed" for severity of urinary symptoms in women.

The tables 4 and 5 provide an overview of the classification of the scales according to criteria

Discussion

There are few validated questionnaires on urinary autonomic symptoms that can be recommended for use in the PD population.

Urinary symptoms are included within autonomic or non-motor symptoms scales for PD - some scales such as the NMSS (severity scale) and NMS-Quest and MDS-UPDRS (screening tools) are well validated and extensively used. However, their use to assess urinary symptoms has the limitation that the number of items is limited and does not assess all LUTS, and there are no data showing that the urogenital subcomponents have adequate clinimetric properties. However they help to detect urinary symptoms which should lead to a more precise evaluation by means of specific questionnaires or a thorough assessment ~~(urodynamics)~~. The SCOPA-AUT covers bladder dysfunction most extensively out of these scales with 6 items on both the voiding and the filling phases.

Studies which aim to investigate bladder dysfunction in PD generally use validated scales designed to assess urological function with more comprehensive urinary items. With the exception of one limited study for the DAN-PSS, the reliability and validity studies of these urological scales have not been conducted specifically in PD patients yet. However

most of them have been shown to correlate with PD disease severity and/or have been used to assess treatment effects of urinary function in PD. Therefore, even if validation of these scales/questionnaires is lacking in PD population, these validated scales/questionnaires used in PD were classified as "Recommended with caveats "with further validation in PD required.

Amongst the generic urinary function scales the ICIQ-MLUTS, DAN-PSS and OAB-q, OAB-q SF and OABSS scales were "Recommended with Caveats". The ICIQ-MLUTS (formerly the ICS male SF) is considered –a comprehensive tool to evaluate LUTS in research and clinical practice, and has also been used in male and female PD patients. The ICIQ-FLUTS (female counterpart for the ICIQ-MLUTS) may be the most pertinent tool for use among females with PD. However a lot of the same items are included in both the male and female versions. The DAN-PSS initially designed for BPH also provides a comprehensive assessment of LUTS. The ICIQ-MLUTS and DAN-PSS both assess a large spectrum of LUTS and bother scores for individual symptoms. The ICIQ has a track record for developing high quality, psychometrically robust questionnaires in this field and considers patients' and healthcare practitioners' perspectives intrinsic to their development.

The well validated OAB-q, OAB-q SF and OABSS have been used in PD populations since OAB symptoms are common in these patients; these questionnaires also assess the related QoL; they have been used in clinical trials. However the OAB questionnaires don't assess all LUTS; some studies showed that their use combined with another questionnaire such as IPSS or DAN-PSS allowed a more comprehensive evaluation of bladder dysfunction. Indeed the selection of the scale/questionnaire must take into account both the goal of its use (clinical practice *vs* clinical trial/ screening *vs* severity assessment/ kind of symptoms) and its characteristics.

Amongst Suggested and Recommended scales, LUTS-related quality of life which is of great importance to patients is considered only in generic urinary function scales.

In addition the different questionnaires do not analyse specifically nocturnal polyuria which can be a cause for nocturia in PD which is a limitation. Micturition flow chart (bladder diary) including measurement of voiding volumes, even it is not strictly a questionnaire, can be used in PD to better evaluate nocturnal polyuria.

All described scales/questionnaires however need to be used further in both longitudinal and cross-sectional studies in PD patients, even the ones recommended for use.

Conclusion

In conclusion, there is no 'off the shelf' instrument for evaluation in a PD population for urinary symptoms that has sufficient clinimetric validity and contains all relevant items for evaluation. Given the length of time and cost involved in developing an entirely new questionnaire we suggest that the ICIQ questionnaires and the DAN-PSS should be evaluated further.

Appendix

In addition to Pablo Martinez, Anette Schrag and Glenn Stebbins, other Members of the MDS Committee on Rating Scales Development Esther Cubo, Deborah Hall, Sheng Luo, Johan Marinus, Laura Marsh and Matej Skorvanek also reviewed the manuscript.

The authors confirm that they have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. The authors confirm that the approval of an institutional review board was not required for this work.

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Table 1: Scales or questionnaires designed to assess non-motor or autonomic symptoms

Scale or questionnaire and reference	**Reference study**	**Number of questions relating to bladder dysfunction**
Severity scales		
SCOPA – AUT (11)	140 PD patients and 100 controls	6 (both filling and voiding phase)
NMSS(12)	242 PD patients multinational	3 (only relating to urgency, frequency and nocturia)
COMPASS (13) *	41controls, 33 patients with non autonomic peripheral neuropathy, 39 patients with autonomic failure (9 PAF, 4 PK plus, 2 MSA)	3
Questionnaire on «Pelvic organ dysfunction in PD» (3)	115 patients with PD and 391 controls; 52 men and 63 women, age 35-69 (average 59) years old, average duration of illness 6 years, median Hoehn and Yahr stage	9 (both filling and voiding phases)
Questionnaire on« Autonomic dysfunction in PD » (17)	44 patients with PD and 24 controls	7 (both filling and voiding phases)
Questionnaire on «Bladder and autonomic dysfunction in PD » (18)	sample of patients with PD (n=123) and elderly controls without PD (n=92)	9 (both filling and voiding phases) based also on Berrios' et al scale + 2 items on QoL related to bladder dysfucntion
Screening tools		
NMS Quest (14)	123 PD patients and 96 controls	2 (only relating to urgency, frequency and nocturia)
MDS-UPDRS –part I (15)	877 patients with PD	1 including 3 sub-items (urgency, frequency, urine accidents)
Questionnaire on « Symptoms of autonomic failure in PD » (16)	141 patients with PD and 50 healthy age-matched control subjects	4 (includes filling but not voiding phase and also has QoL)

MSA: Multiple System Atrophy; PAF: Pure Autonomic Failure; PK: Parkinsonian syndrome ;QoL: Quality of Life.

All the scales were specifically designed for PD patients except COMPASS* which was the only scale designed to assess autonomic symptoms in general medical conditions

Table 2: Clinimetric properties of scales or questionnaires designed to assess non-motor or autonomic symptoms

Clinimetric properties	**SCOPA AUT**	**NMSS**	**QPOD IN PD**	**QAD in PD**	**QBAD in PD**	**NMS Quest**	**MDS-UPDRS**	**QSAF IN PD**	**COMPASS***
Content validity	✓	✓	✓	✓	✓	✓	✓	✓	✓
Comprehension readability	✓	✓	×	×	×	✓	✓	×	≈
Construct validity	✓	≈	×	×	×	✓	✓	×	✓
Floor ceiling effects	✓	✓	×	×	×	✓	✓	×	×
Internal consistency	✓	✓	×	×	×	×	✓	×	×
Test-retest reliability	✓	✓	×	×	×	×	✓	×	×
Factor analysis	✓	✓	×	×	×	×	✓	×	×
Responsiveness	≈	✓	×	×	×	N/A	✓	×	×
MCID	×	✓	×	×	×	N/A	✓	×	×
Time/ administration burden	10 min	10-15 min	×	×	×	5-7 min	<10 min part I 30 min whole scale	5min	<30 min

QPOD in PD: Questionnaire on «Pelvic Organ Dysfunction in PD» (3)
QAD in PD: Questionnaire on« Autonomic dysfunction in PD » (17)
QBAD in PD: Questionnaire on «Bladder and Autonomic Dysfunction in PD » (18)
QSAF in PD: Questionnaire on « Symptoms of Autonomic Failure in PD » (16)
✓ = Fully evaluated
× = Not evaluated
≈ = Some evidence of validation but further evaluation required
MCID = Minimal clinically important difference
All these scales were specifically designed for PD patients. except COMPASS*which was the only scale designed to assess autonomic symptoms in general medical conditions
For each scale, the clinimetric properties have been evaluated on data based on autonomic or non-motor symptoms. However, to our knowledge, there are no data showing that the subcomponents related to urogenital autonomic symptoms have sufficient clinimetric strengths.

Table 3: Clinimetric properties of clinical scales used in urological disorders and applied to PD patients

Clinimetric properties	**IPSS**	**DAN-PSS GENERAL**	**DAN-PSS PD**	**ICIQ-MLUTS/ /ICS Male SF**	**OAB q**	**OAB q SF /ICIQ-OABqol**	**OAB q V8**	**OABSS**	**UDI (short form)**
Content validity	✓	✓	✓	✓	✓	✓	✓	✓	✓
Comprehension readability	✓	✓	✓	✓	✓	✓	✓	✓	✓
Construct validity	✓	✓	✓	✓	✓	✓	✓	✓	≈
Floor ceiling effects	×	×	×,	✓	✓	×	×	×	×
Internal consistency	✓	✓	✓	✓	✓	✓	✓	✓	✓
Test-retest reliability	✓	✓	✓	✓	✓	✓	✓	✓	×
Factor analysis	×	×	×	✓	✓	×	×	×	✓
Responsiveness	✓	✓	×	✓	✓	✓	✓	✓	✓
MCID	×	×	×	×	×	×	×	×	×
Time/ administration burden	< 15 min	Easy to score and quick	Easy to score and quick	Quick	A few minutes	Quick	Very quick	A few minutes	Quick

✓ = Fully evaluated
× = Not evaluated
≈ = Some evidence of validation but further evaluation required
MCID = Minimal clinically important difference.
The questionnaires/scales listed in this table on bladder dysfunction have been fully validated for urological disorders such as benign prostatic hyperplasia and incontinence and then used in PD patients. This table shows the clinimetric properties of the questionnaires/scales in these urological conditions not in PD patients (no data available except for DAN-PSS (54) – see corresponding column and text)

Table 4: Classification of scales or questionnaires designed to assess non-motor or autonomic symptoms

PD-SPECIFIC SCALES TO ASSESS DYSAUTONOMIA OR NMS	Use in PD	Use beyond original developers	Successful clinimetric testing	Clinical advantages and limits	**Classification**
SCOPA-AUT	X	X	No data showing that clinimetric properties for urinary items .	Autonomic symptoms scale. Specifically designed for PD.	**Suggested to assess the severity of urinary symptoms as a part of autonomic symptoms**
NMSS	X	X	No data showing that clinimetric properties for urinary items.	Non motor symptoms scale. Specifically designed for PD. Do not distinguish storage and voiding symptoms	**Suggested to assess the severity of urinary symptoms as a part of autonomic symptoms**
NMS QUEST	X	X	No data showing that clinimetric properties for urinary items.	Non motor symptoms Specifically designed for PD /Screening tool not rating scale. Do not distinguish storage and voiding symptoms	**Suggested as a screening tool to assess urinary symptoms as a part of general autonomic symptoms**
MDS-UPDRS	X	X	Not validated as a single item on urinary symptoms.	General PD symptoms scale /only one item. Do not distinguish storage and voiding symptoms	**Suggested as a screening tool to assess urinary symptoms as a part of non-motor experiences of daily living.**
«PELVIC ORGAN DYSFUNCTION IN PD» (3)	X			Assesses most bladder disorders which may occur in PD /not validated.	**Listed to assess the severity of urinary symptoms as a part of pelvic organ dysfunction**
«AUTONOMIC DYSFUNCTION IN PD» (19)	X			Autonomic symptoms scale designed for PD /small sample size of the study.	**Listed to assess the severity of urinary symptoms as a part of autonomic symptoms**
«BLADDER AND AUTONOMIC DYSFUNCTION IN PD » (20)	V			Autonomic symptoms scale designed for PD mainly focused on bladder dysfunction.	**Listed to assess the severity of urinary symptoms as a part of autonomic symptoms**
« SYMPTOMS OF AUTONOMIC FAILURE IN PD » (18)	X			Autonomic symptoms scale designed for PD.	**Listed as a screening tool to assess urinary symptoms as a part of general autonomic symptoms**
GENERAL MEDICAL SCALES TO ASSESS DYSAUTONOMIA					
COMPASS	X *		Needs more validation. No data showing that clinimetric properties for urinary items.	Autonomic symptoms scale. Comprehensive autonomic assessment/ Needs further validation in PD	**Listed to assess the severity of urinary symptoms as a part of autonomic symptoms**

Table 5: Classification of clinical scales used in urological disorders and applied to PD patients.

Urinary scales applied to PD	**Use in PD**	**Use beyond original developers**	**Successful clinimetric testing**	**Clinical limits/ advantages**	**Classification**
IPSS	X	X µ	X in non-PD. Very limited clinimetric data in PD.. Not enough sensitive to change in PD	Brief – one Qol item – excludes incontinence	**Suggested**
Dan-PSS	X	X µ	X in non-PD. One limited study with clinimetric data in PD. considered as a valuable tool	Includes incontinence and QoL-More sensitive than the IPSS	**Recommended with caveats - Further validation in PD required**
ICIQ-MLUTS (ICS male SF)	X	X µ International questionnaire	X in non PD. No clinimetric data in PD.	Applicable to males and females / assesses all LUTS	**Recommended with caveats Further validation in PD required**
OAB q	X	X µ International questionnaire	X in non PD. No clinimetric data in PD.	Applicable to males and females / focused on OAB	**Recommended with caveats Further validation in PD required**
OAB q SF (ICIQ – OABqol)	X	X µ International questionnaire	X in non PD. No clinimetric data in PD.	Applicable to males and females / focused on OAB	**Recommended with caveats Further validation in PD required**
OAB-V8	X	X µ International questionnaire	X in non PD. No clinimetric data in PD.	Applicable to males and females / focused on OAB Screening tool	**Recommended with caveats Further validation in PD required Screening tool**
OABSS	X	Xµ	X in non PD. No clinimetric data in PD.	Applicable to males and females / focused on OAB	**Recommended with caveats Further validation in PD required**
UDI (short form)	Only one study in PD. No clear results in PD	X µ	X in non PD. No clinimetric data in PD.	Use mainly in women.	**Listed. Additional studies in PD needed**

µ: Use beyond developers mainly in non PD patients - *: validated in non PD patients
All these scales have been designed to assess the severity of urinary symptoms

Authors' Roles

(as follows :
1) Research project: A. Conception, B. Organization, C. Execution;
2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3) Manuscript: A. Writing of the first draft, B. Review and Critique.)

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Nikki Cotterill : 1 C; 2 A, B, C; 3 A, B
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Christopher G. Goetz: 1 A; 2 C; 3 B
Werner Poewe : 1 A; 2 C; 3 B
Cristina Sampaio : 1 A; 3 B
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