



UvA-DARE (Digital Academic Repository)

Role of voiding and storage symptoms for the quality of life before and after treatment in men with voiding dysfunction

Sountoulides, P.; van Dijk, M.M.; Wijkstra, H.; de la Rosette, J.J.M.C.H.; Michel, M.C.

DOI

[10.1007/s00345-009-0480-3](https://doi.org/10.1007/s00345-009-0480-3)

Publication date

2010

Document Version

Final published version

Published in

World journal of urology

[Link to publication](#)

Citation for published version (APA):

Sountoulides, P., van Dijk, M. M., Wijkstra, H., de la Rosette, J. J. M. C. H., & Michel, M. C. (2010). Role of voiding and storage symptoms for the quality of life before and after treatment in men with voiding dysfunction. *World journal of urology*, 28(1), 3-8. <https://doi.org/10.1007/s00345-009-0480-3>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (<https://dare.uva.nl>)

Role of voiding and storage symptoms for the quality of life before and after treatment in men with voiding dysfunction

Petros Sountoulides · Marleen M. van Dijk ·
Hessel Wijkstra · Jean J. M. C. H. de la Rosette ·
Martin Christian Michel

Received: 1 July 2009 / Accepted: 26 September 2009 / Published online: 9 October 2009
© The Author(s) 2009. This article is published with open access at Springerlink.com

Abstract

Purpose Previous studies on associations between voiding dysfunction and quality of life (QoL) have largely been limited to baseline data. Therefore, we have explored associations between Q_{\max} and voiding and storage sub-scores of the International Prostate Symptom Score (IPSS) before and after treatment with QoL.

Methods Analysis of a single-center database of 2,316 men with voiding dysfunction attributed to benign prostatic hyperplasia undergoing various medical and surgical treatment forms.

Results Q_{\max} exhibited little correlation with QoL before or after treatment. IPSS inversely correlated with QoL at baseline and after treatment, and IPSS improvements correlated with those of QoL. The associations applied to both the voiding and storage sub-score of the IPSS, with the latter consistently exhibiting somewhat tighter associations.

Conclusions Our post-treatment data support the idea of a cause–effect relationship between voiding symptoms and QoL irrespective of treatment form. While both voiding and storage symptoms contribute to this relationship, storage symptoms play a somewhat greater role.

Keywords Quality of life · Benign prostatic hyperplasia · Voiding dysfunction · α -Blocker · Transurethral microwave thermotherapy · Transurethral resection of the prostate

Introduction

Male voiding dysfunction is common in the general population, particularly in the elderly. It is often, although not necessarily rightly so, attributed to the presence of benign prostatic hyperplasia (BPH). The extent of voiding dysfunction is typically assessed by quantifying signs such as a reduced peak urinary flow (Q_{\max}) or symptoms as measured in the International Prostate Symptom Score (IPSS). Based upon factor analysis [1], the IPSS is often subdivided into a voiding and a storage sub-score. Of note, the IPSS is somewhat biased toward voiding symptoms, as four of the seven question belong to the voiding sub-score. While a pathophysiological link between BPH and the associated obstruction and lower urinary tract symptoms (LUTS) implies mainly the presence of voiding/obstructive symptoms, storage/irritative symptoms are also common in such men [2].

Male LUTS are often associated with a reduced disease-specific quality of life (QoL). This can be assessed by a variety of questionnaires among which the QoL question of the IPSS is used most often [3] although more complex instruments such as the SF-36 questionnaire may be more informative [4]. Such research shows that a greater IPSS statistically is strongly associated with a reduced QoL prior to treatment [5, 6]. Many studies imply that storage symptoms may contribute to this reduced QoL to a greater extent than voiding symptoms across both genders [4, 7–10], even among men considered to have major obstruction as they are waiting for BPH-related surgery [11] but limited other

P. Sountoulides and M. M. van Dijk contributed equally to this work.

P. Sountoulides · M. M. van Dijk · H. Wijkstra ·
J. J. M. C. H. de la Rosette
Department of Urology, Academic Medical Center,
Amsterdam, The Netherlands

M. C. Michel (✉)
Department of Pharmacology and Pharmacotherapy,
Academic Medical Center, Meibergdreef 15,
1105 AZ Amsterdam, The Netherlands
e-mail: m.c.michel@amc.uva.nl; M.C.Michel@amc.nl

studies in men report a stronger association of voiding than storage symptoms with a reduced QoL [12]. Whether a reduced Q_{\max} and voiding symptoms as assessed in the IPSS and its voiding sub-score can be considered equivalent in this regard has not been evaluated thoroughly.

Thus, the existing literature clearly demonstrates an association of both voiding and storage symptoms with QoL at baseline, with the latter exhibiting somewhat stronger correlations. However, a cause–effect relationship is difficult to evaluate based upon statistical associations at baseline alone. Stronger scientific arguments could come from analysis of similar relationships after treatment but only very limited data on this are available [13]. Even more importantly, evidence for a cause–effect relationship could come from exploring associations between treatment-associated changes of voiding and storage sub-scores on the one and changes of QoL on the other hand. While various treatment forms have consistently shown QoL improvement in LUTS/BPH patients [14], the relationship between improvements of voiding and storage sub-scores with those of QoL, to the best of our knowledge, has not been studied before. Therefore, the present study was done to primarily explore such relationships after treatment in a large sample of men with LUTS/BPH.

Patients and methods

This is a retrospective analysis of a single-center database generated during routine care at the Dept. of Urology of the Radboud University Nijmegen Medical Centre (Nijmegen, Netherlands), which includes patients diagnosed with LUTS/BPH between 1992 and 2002. The diagnosis and treatment decisions were not based on formalized criteria but on the medical judgment of one urologist (JdIR) based upon digital rectal examination, estimation of prostate volume by means of transrectal ultrasound, uroflowmetry, urinalysis and IPSS including its QoL question.

Our analysis of associations at baseline includes all patients in the database for whom relevant data were available ($n = 2,611$). Post-treatment analyses are based on patients with at least one assessment of the IPSS 6–12 months after initiation of treatment where at least 150 patients were available for a given form of treatment. This time frame was chosen because it should yield a reasonably stable post-treatment situation. The following interventions yielded sufficient patient numbers for further analysis: watchful waiting (WW, $n = 421$), α -blockers ($n = 297$), transurethral microwave thermotherapy (TUMT, $n = 356$) and transurethral resection of the prostate (TURP, $n = 184$). This excluded 696 patients because they had received treatments other than the above, and 265, 198, 72 and 122 in the WW, α -blockers, TUMT and TURP groups, respectively,

because no post-treatment data were available. α -Blocker treatment consisted of standard doses of alfuzosin, tamsulosin or terazosin. TUMT was administered with the Prostatron machine (EDAP-TMS, France) on an ambulatory basis, and TURP was performed under spinal or general anesthesia. If more than one assessment was done within 6–12 after initiation of treatment, the results closest to 9 months after initiation were used.

A descriptive analysis of the treatment groups at baseline and after 6–12 months of treatment is presented as mean \pm SD. From the IPSS a voiding sub-score based upon the symptoms incomplete emptying, intermittency, weak stream, and straining was calculated and a storage sub-score based upon frequency, urgency, and nocturia [1]. As both the voiding and the storage sub-score of the IPSS correlated only poorly with Q_{\max} at baseline ($r = 0.162$ and 0.126 , respectively, $n = 2611$), we have used all three parameters in parallel as explanatory variables to explore their relationships with QoL using multiple regression analysis. Specifically, we have addressed three questions: (1) What is the statistical association of Q_{\max} and the voiding and storage sub-score to QoL at baseline and after 6–12 months of treatment (secondary aim)? (2) Do the various treatments differ in their effects on Q_{\max} , voiding and storage (tertiary aim)? For this analysis, the possibly confounding factors age, and baseline values of the respective parameter were used as covariates in a multiple regression analysis. Moreover, the α -blocker group was used as the reference treatment because most data from double-blind, randomized studies exist for this treatment form which is known to improve voiding and storage sub-scores to a similar extent [15–23]. (3) What is the statistical association of the treatment-associated alterations of Q_{\max} , voiding and storage sub-scores to the associated improvement in QoL score (primary aim)? All statistical analyses were performed with the statistical software SPSS for Windows (version 11.5.1, SPSS Inc. Chicago, IL, USA.), and a $p < 0.05$ was considered as statistically significant.

Results

In multiple regression analysis, baseline Q_{\max} and voiding and storage sub-scores of the IPSS were significantly but weakly associated with QoL with the storage sub-score exhibiting the strongest association among the three explanatory variables (Table 1). Thus, all other factors being equal, a Q_{\max} difference of 1 ml/s or 1 point in each sub-score statistically explained only a difference of 0.010, 0.074 and 0.120 points in the QoL score.

As expected, patients assigned to WW, α -blocker, TUMT and TURP had different baseline characteristics. Lower baseline Q_{\max} correlated with increasing invasiveness

Table 1 Multiple regression analysis of the relationship between Q_{\max} , voiding and storage score on the one and QoL on the other hand

Parameter	Baseline	Post-treatment	Change parameter vs. change QoL
Q_{\max} , per ml/s	-0.010 ± 0.004	-0.016 ± 0.004	-0.033 ± 0.005
Voiding sub-score, per point	0.074 ± 0.005	0.107 ± 0.007	0.109 ± 0.008
Storage sub-score, per point	0.120 ± 0.006	0.156 ± 0.010	0.119 ± 0.012

The analysis is based upon 2,316 and 1,258 patients prior to and 6–12 months after treatment, respectively. Data are given as unstandardized regression coefficients with SEM (all $p < 0.05$) at baseline, after treatment and for the association between Q_{\max} and score changes with those of QoL

of treatment chosen, i.e. was highest in the WW and lowest in the TURP group (Table 2). The voiding and storage sub-scores at baseline were lower in the WW than in the other three groups, but no major differences were seen between the latter three.

Increasing invasiveness of treatment was associated with increasing improvements of Q_{\max} and voiding and storage sub-scores (Table 2), i.e. all three parameters improved with an order of effectiveness of WW < α -blocker < TUMT < TURP. In order to explore in more detail the relationship between a form of treatment and the extent of improvement of Q_{\max} and voiding and storage sub-scores, we have applied multiple regression analysis using age and baseline value of the respective parameter as co-explanatory variables (Table 3). This analysis demonstrated small but significant adverse effects of age on the improvement of Q_{\max} and the storage sub-score, whereas improvements of the voiding sub-score were not significantly affected. As expected, respective baseline values had a strong effect on the improvement of all three parameters, i.e. each ml/s or point at baseline statistically explained approximately 0.5 ml/s or 0.6 points of improvement. Compared to α -blocker treatment as the reference group, WW had rather similar effects, i.e. they were numerically slightly weaker than those of the α -blocker with the differences reaching statistical significance only for the voiding sub-score. In contrast, TUMT and even more so TURP yielded greater benefit than α -blocker treatment. Interestingly, these differences were more pronounced for Q_{\max} and the voiding than for the storage sub-score.

Having characterized the effects of the various treatments on Q_{\max} and the IPSS sub-scores, we have applied

multiple regression analysis to explore their associations with QoL after treatment (Table 1). This confirmed the associations between all three parameters and QoL already observed at baseline. Finally, and most importantly, we have explored our primary research question, i.e. how treatment-associated alterations of Q_{\max} and voiding and storage sub-scores related to alterations of QoL (Table 1). Improvements of all three parameters were significantly but weakly associated with QoL improvements. For example, each treatment-induced change of Q_{\max} by 1 ml/s or the voiding or storage sub-score by 1 point was associated with changes of QoL by 0.033, 0.109 and 0.119 points, respectively.

Discussion

The present analysis was primarily designed to explore whether the hypothesis of LUTS as a cause of reduced QoL and specifically the relative roles of voiding and storage LUTS can be further supported by post-treatment data.

Critique of methods

For the selection of post-treatment data we have limited ourselves to patients with at least one assessment at 6–12 months after initiation of treatment to reflect a somewhat stable clinical situation. Moreover, we have limited ourselves to patients which had received one of the treatment forms for which at least 150 patients were available to yield meaningful group sizes. Patients with and without follow-up data did not differ in a meaningful way in their baseline

Table 2 Baseline and post-treatment characteristics according to allocated treatment

	Watchful waiting	α -blocker	TUMT	TURP
<i>n</i>	421	297	356	184
Age (years)	62.9 ± 7.8	62.6 ± 8.0	67.1 ± 8.1	64.9 ± 7.4
Q_{\max} (ml/s)	12.5 ± 5.6	10.7 ± 5.0	9.3 ± 3.3	8.3 ± 3.4
	$+2 \pm 43\%$	$+14 \pm 53\%$	$+80 \pm 140\%$	$+217 \pm 220\%$
Voiding sub-score, points	7.8 ± 4.3	10.6 ± 4.4	10.7 ± 4.4	10.9 ± 4.4
	$+2 \pm 85\%$	$-28 \pm 51\%$	$-60 \pm 45\%$	$-85 \pm 24\%$
Storage sub-score, points	5.8 ± 3.2	7.9 ± 3.2	8.3 ± 3.3	8.3 ± 3.3
	$-2 \pm 69\%$	$-25 \pm 41\%$	$-38 \pm 49\%$	$-60 \pm 30\%$

Data are mean \pm SD of the indicated number of patients for baseline values and % changes thereof upon 6–12 months of treatment

Table 3 Multiple regression analysis of the relationship between form of treatment and other factors and improvement of the Q_{\max} and voiding and storage sub-scores of the IPSS

Variable	Q_{\max} , ml/s	Voiding sub-score, points	Storage sub-score, points
Age, per year	-0.083 ± 0.022	0.003 ± 0.014	0.035 ± 0.010
	<0.001	0.826	<0.001
Basal value	-0.452 ± 0.037	-0.675 ± 0.025	-0.590 ± 0.023
	<0.001	<0.001	<0.001
Watchful waiting	-0.259 ± 0.461	0.770 ± 0.295	0.303 ± 0.208
	0.574	0.009	0.145
TUMT	4.222 ± 0.480	-3.060 ± 0.305	-1.301 ± 0.214
	<0.001	<0.001	<0.001
TURP	12.348 ± 0.569	-5.436 ± 0.357	-2.665 ± 0.250
	<0.001	<0.001	<0.001

Data are mean \pm SEM of the unstandardized regression coefficient and the corresponding p -values. Effects of treatment forms are expressed relative to those of the reference group (α -blocker treatment). This means e.g. that all other factors being equal, 1 year of age explains an improvement of the storage sub-score by 0.035 points, one point of the voiding sub-score at baseline explains an improvement of this sub-score by 0.675 points, and that TURP improves the storage sub-score by 2.665 points more than α -blocker treatment

values, and all treatment groups had comparable attrition rates (data not shown). Treatment allocations had been based upon the clinical judgment of one urologist, yielding the expected heterogeneity in pre-treatment symptoms between groups. Where applicable this has been taken account as co-variables in our analyses, as randomized comparisons of e.g. WW and TURP would be neither feasible nor ethical [24].

Our QoL assessments are based upon the QoL question of the IPSS. While more complex instruments such as the SF-36 may have benefits over single-item questionnaires, the QoL question of the IPSS has been used in the majority of previous studies in the field and consistently shown good correlations with more complex instruments and hence is considered to be a valid QoL assessment with major utility due to its simplicity [14].

Multiple biological mechanisms including degeneration of the bladder upon long-standing obstruction may contribute as causes of LUTS and hence QoL, but the present database does not allow this type of analysis.

In line with previous studies [25, 26] our analysis showed only limited correlation between both voiding or storage sub-scores with Q_{\max} , and hence Q_{\max} has been included as a separate item into our analyses. All of these factors should be taken into account in the interpretation of our data.

Baseline data

In line with many previous studies [4, 7–11], our baseline data confirm that the storage sub-score exhibits a somewhat stronger association with QoL than the voiding sub-score and each of them a stronger association than Q_{\max} . The extent of the difference in strength of association between

the voiding and storage sub-scores may even be under-estimated because the IPSS is biased toward voiding symptoms [1] and hence one point of the storage sub-score is somewhat more difficult to achieve than one point of the voiding sub-score. This validates our database and findings for the subsequent analysis of post-treatment data.

Treatment effects

As expected, the various treatment forms varied considerably in their efficacy with the more invasive treatments (TUMT, TURP) causing greater improvement than α -blockers despite similar baseline symptoms. Of note, the superiority of TUMT and TURP related not only to the voiding but also, albeit to a slightly smaller extent, to the storage symptoms. Possible roles of more recent medical approaches to LUTS, particularly storage LUTS, such as muscarinic receptor antagonists [27] could not be evaluated as part of our studies as none of our patients had received such medication.

A statistical association of two parameters at baseline provides only very limited evidence for a cause–effect relationship. Therefore, the main aim of the present analysis was to explore the statistical associations of voiding and storage symptoms with QoL after treatment, and even more importantly how well improvements in either sub-score correlate to those of QoL. Very limited earlier findings have indicated that storage symptoms correlate somewhat better with QoL than voiding symptoms, with Q_{\max} yielding little association [13]. Our data, based upon multiple treatment forms with different efficacy, confirm those findings. Our data importantly extend those earlier studies by demonstrating that reductions of both voiding and storage sub-scores correlate with QoL improvements, with the latter yielding

somewhat tighter associations. As with the baseline data, the extent of the difference in strength of association between the voiding and storage sub-scores may even be under-estimated because the IPSS is biased toward voiding symptoms [1]. In contrast, Q_{\max} shows only little association with QoL after treatment.

Conclusions

While many previous studies have demonstrated inverse correlations between voiding and storage symptoms and QoL at baseline, our study for the first time shows that improvements of symptoms correlate with improvements of QoL. This considerably strengthens the logical assumption that symptoms and QoL are indeed related in a cause-effect relationship. Our study also shows that both voiding and storage symptoms correlate with QoL with the latter exhibiting slightly tighter correlations, and that such association can be found not at baseline but also after treatment. The relevance of this conclusion is underscored by its apparent applicability to various medical and surgical treatment forms.

Conflict of interest statement The authors report no conflict of interest related to this manuscript.

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

1. Welch G, Kawachi I, Barry MJ et al (1998) Distinction between symptoms of voiding and filling in benign prostatic hyperplasia: findings from the health professionals follow-up study. *Urology* 51:422–427
2. Kaplan SA, Roehrborn CG, Chapple CR et al (2009) Implications of recent epidemiology studies for the clinical management of lower urinary tract symptoms. *BJU Int* 103(Suppl 3):48–57
3. Donovan JL (2000) The measurement of symptoms, quality of life and sexual function. *BJU Int* 85(Suppl 1):10–19
4. Engström G, Henningsohn L, Walker-Engström M-L et al (2006) Impact on quality of life of different lower urinary tract symptoms in men measured by the Short Form 36 SF 36 questionnaire. *Scand J Urol Nephrol* 40:485–494
5. Tubaro A, La Vecchia C (2004) The relation of lower urinary tract symptoms with life-style factors and objective measures of benign prostatic enlargement and obstruction: an Italian survey. *Eur Urol* 45:767–772
6. Robertson C, Link CL, Onel E et al (2007) The impact of lower urinary tract symptoms and comorbidities on quality of life: the BACH and UREPIK studies. *BJU Int* 99:347–354
7. Peters TJ, Donovan JL, Kay HE et al (1997) The International Continence Society “benign prostatic hyperplasia” study: the bothersomeness of urinary symptoms. *J Urol* 157:885–889
8. Yoshimura K, Arai Y, Ichioka K et al (2002) Symptom-specific quality of life in patients with benign prostatic hyperplasia. *Int J Urol* 9:485–490
9. Coyne KS, Wein AJ, Tubaro A et al (2009) The burden of lower urinary tract symptoms: evaluating the effects of LUTS on health-related quality of life, anxiety and depression: EpiLUTS. *BJU Int* 103(Suppl 3):4–11
10. Sexton CC, Coyne KS, Kopp ZS et al (2009) The overlap of storage, voiding and postmicturition symptoms and implications for treatment seeking in the USA, UK and Sweden: EpiLUTS. *BJU Int* 103(Suppl 3):12–23
11. Salinas-Sanchez AS, Hernandez-Millan I, Lorenzo-Romero JG et al (2001) Quality of life of patients on the waiting list for benign prostatic hyperplasia surgery. *Quality Life Res* 10:543–553
12. Araki I, Tsuchida T, Nomura T et al (2008) Differential impact of lower urinary tract symptoms on generic and disease-specific quality of life in men and women. *Urol Int* 81:60–65
13. Marklund-Bau H, Edell-Gustafsson U, Spangberg A (2007) Bothersome urinary symptoms and disease-specific quality of life in patients with benign prostatic obstruction. *Scand J Urol Nephrol* 41:32–41
14. Batista-Miranda JE, De la Cruz Diez M, Arano Betran P et al (2001) Quality-of-life assessment in patients with benign prostatic hyperplasia. Effects of various interventions. *Pharmacoeconomics* 19:1079–1090
15. Lepor H, Auerbach S, Puras-Baez A et al (1992) A randomized, placebo-controlled multicenter study of the efficacy and safety of terazosin in the treatment of benign prostatic hyperplasia. *J Urol* 148:1467–1474
16. Fabricius PG, Hannaford JM (1992) Placebo-controlled study of terazosin in the treatment of benign prostatic hyperplasia with 2-year follow up. *Urology* 70(Suppl 1):10–16
17. Chapple CR, Wyndaele JJ, Nordling J et al (1996) Tamsulosin, the first prostate-selective α_{1A} -adrenoceptor antagonist. A meta-analysis of two randomized, placebo-controlled multicentre studies in patients with benign prostatic obstruction (symptomatic BPH). *Eur Urol* 29:155–167
18. Lee E, Lee C (1997) Clinical comparison of selective and non-selective α_{1A} -adrenoceptor antagonists in benign prostatic hyperplasia: studies on tamsulosin in a fixed dose and terazosin in increasing doses. *Br J Urol* 80:606–611
19. Lepor H (1998) Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. *Urology* 51:892–900
20. Kirby RS, Andersen M, Gratzke P et al (2001) A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. *BJU Int* 87:192–200
21. Michel MC, Flannery MT, Narayan P (2001) Worldwide experience with alfuzosin and tamsulosin. *Urology* 58:508–516
22. Roehrborn C, van Kerrebroeck P, Nordling J (2003) Safety and efficacy of alfuzosin 10 mg once-daily in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a pooled analysis of three double-blind, placebo-controlled studies. *BJU Int* 92:257–261
23. Djavan B, Milani S, Davies J et al (2005) The impact of tamsulosin oral controlled absorption system (OCAS) on nocturia and the quality of sleep: preliminary results of a pilot study. *Eur Urol Suppl* 4:61–68
24. Wasson JH, Reda DJ, Bruskewitz RC et al (1995) A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. *New Engl J Med* 332:75–79
25. Yalla SV, Sullivan MP, Lecamwasam HS et al (1995) Correlation of American Urological Association symptom index with obstructive and nonobstructive prostatism. *J Urol* 153:674–680

-
26. NRjr Netto, D'Ancona CAL, de Lima ML (1996) Correlation between the International Prostatic Symptom Score and a pressure-flow study in the evaluation of symptomatic benign prostatic hyperplasia. *J Urol* 155:200–202
27. Lee K-S, Lee HW, Han DH (2008) Does anticholinergic medication have a role in treating men with overactive bladder and benign prostatic hyperplasia? *Naunyn-Schmiedeberg's Arch Pharmacol* 377:491–501