Comparison of IPSS score and voiding parameters in men presenting with LUTS

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Introduction: *This study compares subjective lower urinary tract symptoms (LUTS) to objective voiding parameters measured during the UroCuff Test, a non-invasive pressure flow study (PFS), in men presenting with LUTS attributed to benign prostatic hyperplasia (BPH).*
Materials and methods: *This is an expanded subpopulation analysis of a previously reported group of 50,680 men with LUTS, which depicted increased disease progression as men age. During the UroCuff Test, investigators optionally provided the International Prostate Symptom Score (IPSS).*
Variables were analyzed using descriptive statistics, pairwise correlation coefficients between variables and a multivariable linear regression model fit for IPSS as a continuous outcome.
Results: *IPSS data are available for 1077 patients. Compared to the 50,680 group, men in this subpopulation are similar in age but overall have improved mean values for voided volume (VV), maximum flow rate (Qmax), and less advanced bladder disease by UroCuff quadrant. IPSS has highly statistically significant ($p < 0.001$), but weak correlations with Qmax, VV, post-void residual volume (PVR) and UroCuff quadrant, with correlation coefficients (absolute values) of 0.212, 0.174, 0.151, 0.159, respectively. Multivariable linear regression analysis stratified by UroCuff quadrant demonstrate that increased age and high VV are associated with decreased IPSS, while high PVR is associated with increased IPSS. These relationships become weaker as patients experience increasing disease progression.*
Conclusion: *Since self-reported urological symptoms are only weakly correlated with objective voiding parameters, LUTS diagnosis using IPSS alone is insufficient to create diagnostic certainty. Optimal clinical management of male LUTS depends on a thorough evaluation of both symptoms and voiding parameters.*

Key Words: IPSS, BPH, LUTS, Urodynamics, UroCuff

Introduction

Urologists use evidence-based medicine to address their male patient's lower urinary tract symptoms (LUTS) and prostatic obstruction, and to optimally maintain functional bladders.

As recommended by the American Urological Association (AUA) and by other national urological societies, urologists administer the IPSS to quantify the patient's self-reported symptoms. Diagnostic testing includes both uroflowmetry and pressure flow studies, including UroCuff, to evidence the presence of bladder outlet obstruction (BOO). Previous clinical publications have demonstrated disparity (weak correlations) between the professed symptoms and

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urodynamic measures.[1-5] Authors have questioned whether the weak correlations are an actual disease state phenomenon or are an artifact of study design.

The current AUA Guideline for the Management of Benign Prostatic Hyperplasia / Lower Urinary Tract Symptoms BPH Guideline[6] states that "clinicians should consider pressure flow studies prior to intervention for LUTS/BPH when diagnostic uncertainty exists." UroCuff is a reliable pressure flow study (PFS) that accurately predicts BOO, and has been shown to be highly correlated with catheterized urodynamic testing[7-9] without the technical complexities. It has a high inter-observer agreement that suggests that the UroCuff Test can be carried out by separate clinicians in a standardized manner.[10] The UroCuff Test has automized data capture that allows efficient retrieval of data and facilitated the collection of a data set of 50,680 male LUTS patients.[11] As collection of IPSS was optional, 1077 patients have valid IPSS data.

We quantify the relations between urological symptoms and voiding parameters using a large sample of over 1000 men and discuss the clinical implications of these relationships and the optimal management of men with LUTS.

Materials and methods

UroCuff protocol

UroCuff testing was performed on the CT3000 Series Complete Urodynamics instrument (SRS Medical, North Billerica, MA, USA) simulating conditions of a routine, real-world void. UroCuff patients are instructed to present for the visit with a comfortably full bladder and to begin the test when they have a strong desire to void. The UroCuff protocol and the pre-test instructions designed to optimize the patient's void are detailed elsewhere.[11,12]

Data collection

Protected health information were de-identified before data were extracted directly from the UroCuff device's database and made available for analysis. UroCuff generated data collected for all patients included Qmax, VV, Pcuff, and UroCuff quadrant plotted on the Newcastle Non-invasive Nomogram.[13] Optional UroCuff data were age, IPSS, and PVR, which were entered only by some clinics who wanted these data to print on the UroCuff report. Pcuff is the applied pressure required to interrupt the urine stream during the test and is a measurement consistent with the standard pressure flow study measure of isovolumetric pressure.[14,15] Flow rate efficiency (FRE) is a calculated value, Qmax divided by Pcuff.

Selection criteria

Selection criteria for the analysis of the 50,680 patients are reported elsewhere.[11] This subpopulation differed only by the additional requirement of a valid IPSS.

Statistical analysis

The key variables of interest for this analysis were age, VV, Qmax, PVR, UroCuff quadrant, Pcuff, FRE, and IPSS. Median and IQR are reported for summary statistics. For categorical variables, the relative frequencies and percentages are reported.

The pairwise correlation coefficients between variables of interest were calculated. Pearson's correlation coefficient (Pearson's r) was used to quantify correlation between the continuous variables. Spearman's rho was used to quantify correlations involving UroCuff quadrant and PVR since UroCuff quadrant is an ordinal variable and PVR is highly skewed, Figure 1.

Regression models

Linear regression models of continuous IPSS were fit individually for each variable of interest.

A multivariable linear regression model was fit for IPSS as a continuous outcome and multivariable linear regression models of continuous IPSS were fit separately for each UroCuff quadrant. The predictor variables included in the models were binary indicator variables for age, Qmax, VV, and PVR, and a categorical variable for UroCuff quadrant. The binary indicator variables were determined using the sample median and a categorical variable was used for UroCuff quadrant.

Study oversight

This study was exempt from IRB review per 45 CFR §46.104, and informed consent was not required per 45 CFR §46.116. Registration on ClinicalTrials.gov was not required as this study is not an applicable clinical trial per 42 CFR §11.22.

Results

Subpopulation with IPSS data versus all patients

The IPSS subpopulation has the same age distribution as the overall analysis group but has improved mean values for the voiding parameters VV, Qmax, and UroCuff quadrant.

The subpopulation had a higher proportion of patients presenting in the unobstructed, and in the high pressure/high flow (HP/HF) categories (less advanced in the bladder function lifecycle) and fewer presenting in the obstructed and the low pressure/low flow (LF/LF) categories (more advanced on the

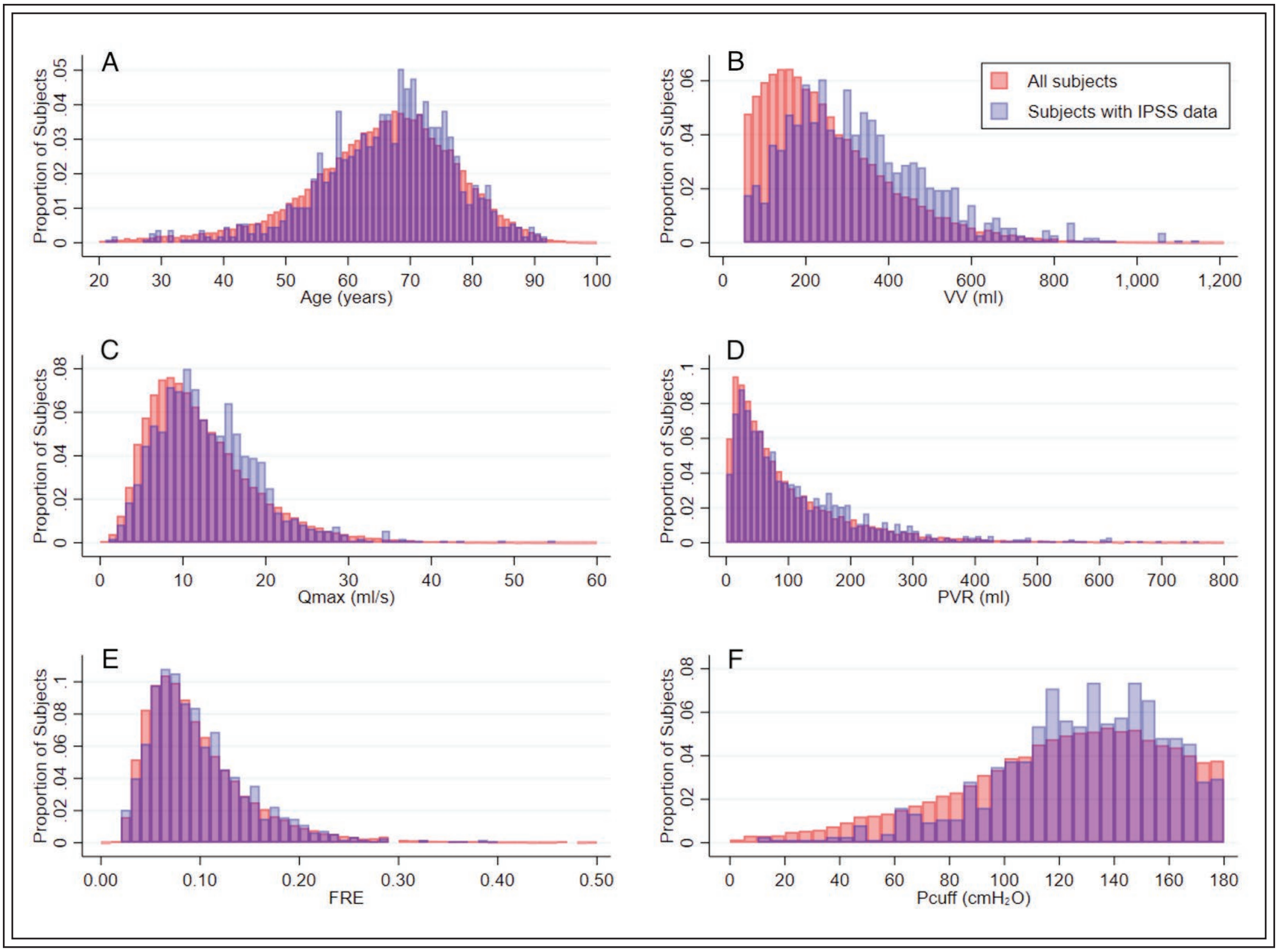

Figure 1. Histograms of subpopulation with IPSS data and all patients. **A)** Age distribution; **B)** voided volume distribution; **C)** Qmax distribution; **D)** PVR distribution; **E)** FRE (flow rate efficiency) distribution; **F)** Pcuff distribution.

bladder function lifecycle), compared to patients in the overall population, Figure 1 and Table 1.

IPSS

The IPSS subpopulation is comprised of 1077 patients. Median reported IPSS was 10.0 and IQR was (6.0, 17.0). The majority (554/1,079; 51%) of patients reported moderate LUTS. Approximately 1/3 of patients (344/1,079, 32%) reported mild LUTS.

Correlation matrix

Correlations between IPSS and voiding parameters: IPSS has statistically significant (all p values < 0.001) but weak correlations with Qmax, VV, PVR, and UroCuff quadrant; the absolute value of each correlation coefficient is less than 0.2, Table 2, Figure 2.

For UroCuff quadrant, each ordinal quadrant (unobstructed, HP/HF, obstructed, LP/LF) was assigned a number 1 through 4 with higher numbers indicating more advanced bladder dysfunction. There is a weak but statistically significant positive correlation between IPSS and UroCuff quadrant ($p < 0.001$, correlation coefficient = 0.159).

Correlations between voiding parameters: Among voiding measures, Qmax has statistically significant (both $p < 0.001$), weak correlations with VV and PVR volume, correlation coefficient = 0.246 and -0.262, respectively. There is no relationship between VV and PVR volume, $p = 0.682$, correlation coefficient = -0.013).

Both FRE and UroCuff quadrant assess the relationship between flow rate and pressure. FRE is calculated as Qmax/Pcuff and interpreted as the amount of pressure required to produce 1 mL of urine, and UroCuff quadrant is determined by plotting Qmax and Pcuff. The two measures demonstrate a strong, statistically significant correlation ($p < 0.001$, correlation coefficient = -0.745).

TABLE 1. **Descriptive statistics, subpopulation with IPSS data versus all patients**

	Subpopulation with IPSS data n = 1077	All patients n = 50680
IPSS		
N	1077	1079
Median (IQR)	10.0 (6.0, 17.0)	10.0 (6.0, 17.0)
Age		
N	1071	50045
Median (IQR)	67.0 (59.0, 73.0)	66.0 (58.0, 73.0)
Voided volume		
N	1077	50680
Median (IQR)	305.0 (203.0, 431.0)	219.0 (138.0, 337.0)
PVR		
N	1014	18806
Median (IQR)	78.0 (36.0, 164.0)	66.0 (30.0, 141.0)
Qmax		
N	1077	50680
Median (IQR)	12.0 (8.7, 16.6)	10.9 (7.5, 15.6)
FRE		
N	1077	50680
Median (IQR)	0.08 (0.06, 0.12)	0.08 (0.6, 0.12)
Pcuff		
N	1077	50680
Median (IQR)	148.7 (119.5, 189.4)	144.3 (109.5, 185.0)
UroCuff quadrant (%) (n/N)		
Unobstructed	27.6% (297/1077)	24.2% (12277/50680)
High pressure/high flow	37.3% (403/1077)	31.6% (16005/50680)
Obstructed	27.4% (295/1077)	29.2% (14820/50680)
Low pressure/low flow	7.7% (84/1077)	15.0% (7578/50680)

IPSS = International Prostate Symptom Score; IQR = interquartile range; PVR = post-void residual volume; Qmax = maximum flow rate; FRE = flow rate efficiency; Pcuff = urine flow interruption pressure

UroCuff quadrant shows a strong negative correlation with Qmax, ($p < 0.001$, correlation coefficient = -0.803) and moderate relationships with VV and PVR, (both $p < 0.001$, correlation coefficient = -0.413 and 0.247 respectively).

Relationship between IPSS category and UroCuff quadrant

Figure 3 depicts the IPSS category distribution for each of the four UroCuff PFS quadrants. Approximately half of the patients in every UroCuff quadrant report moderate symptoms (IPSS 8-19). Mild symptoms (IPSS < 8) are more likely to be reported in unobstructed and HP/HF quadrants, while severe symptoms (IPSS > 19) are more likely to be reported in obstructed and LP/LF quadrants. Although statistically significant, Figure 3 depicts the weak positive correlation between IPSS and UroCuff quadrant.

Regression models, Table 3

Multivariable regression models

Multivariable linear regression analysis stratified by UroCuff quadrant demonstrated that old age and high voided volume were significantly associated with decreased IPSS, while high PVR was associated with increased IPSS, Table 4.

For unobstructed men, being older than 67 was associated with a 2.2-point decrease in IPSS ($p = 0.007$), a VV over 305 mL was associated with a 2.8-point decrease in IPSS ($p = 0.001$) and having a PVR over

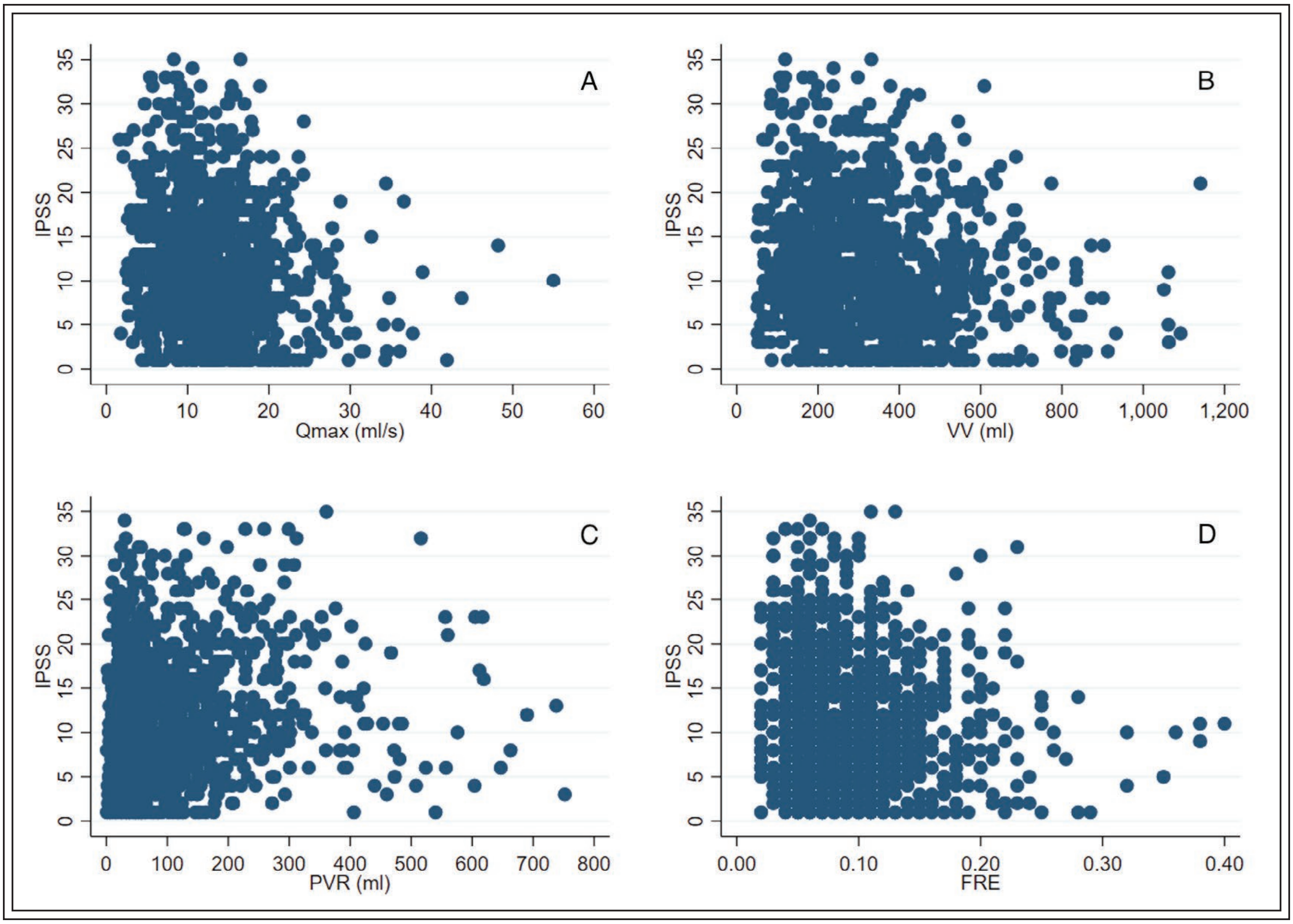

Figure 2. Scatterplot of IPSS in relation to **A)** Qmax; B) voided volume; **C)** PVR; **D)** FRE.

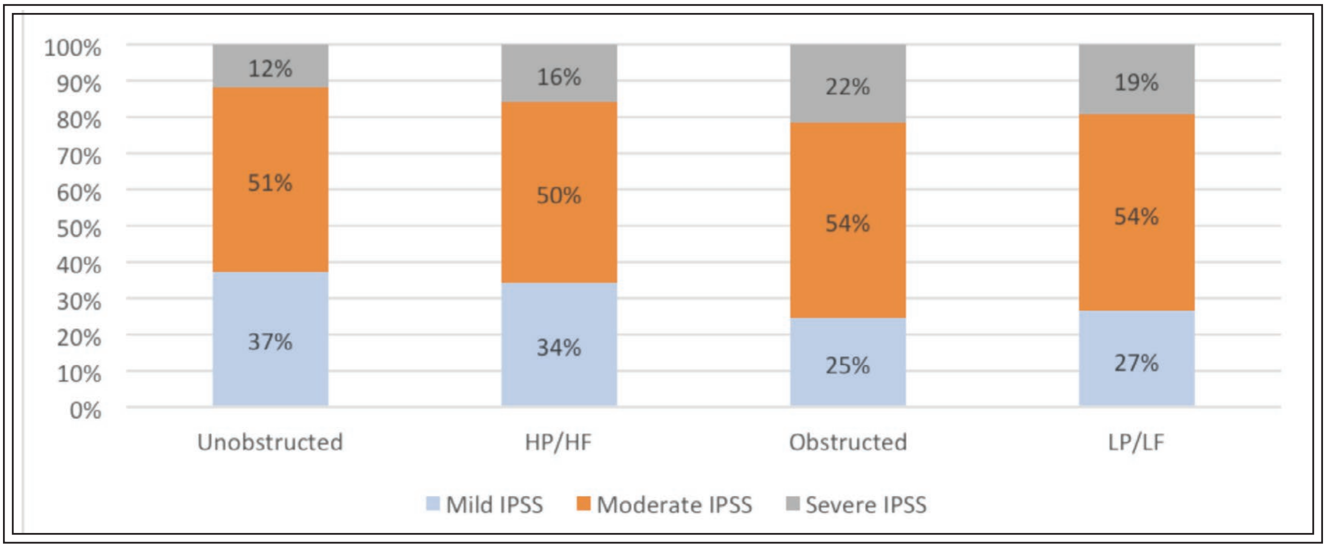

Figure 3. IPSS category percentage per UroCuff quadrant: unobstructed, high pressure/high flow, obstructed, low pressure/low flow.

TABLE 2. **Correlation matrix**

		IPSS	Qmax	VV	PVR	Pcuff	FRE	UroCuff quadrant
IPSS	Pearson's r	1.000						
	p value							
	N	1077						
Qmax	Pearson's r	-0.121	1.000					
	p value	< 0.001						
	N	1077	1077					
VV	Pearson's r	-0.174	0.246	1.000				
	p value	< 0.001	< 0.001					
	N	1077	1077	1077				
PVR	Spearman's rho	0.151	-0.262	-0.013	1.000			
	p value	< 0.001	< 0.001	0.682				
	N	1014	1014	1014	1014			
Pcuff	Pearson's r	0.006	0.010	0.196	0.034	1.000		
	p value	0.843	0.774	< 0.001	0.277			
	N	1077	1077	1077	1014	1077		
FRE	Pearson's r	-0.072	0.876	0.054	-0.252	-0.219	1.000	
	p value	0.018	< 0.001	0.076	< 0.001	< 0.001		
	N	1077	1077	1077	1014	1077	1077	
UroCuff quadrant	Spearman's rho	0.159	-0.803	-0.413	0.247	0.136	-0.745	1.000
	p value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	
	N	1077	1077	1077	1014	1077	1077	1077

Pearson's correlation coefficient (Pearson's r) was used to quantify correlation between the continuous variables IPSS, Qmax, Voided Volume and Pcuff. Spearman's rho was used to quantify correlations involving UroCuff quadrant and PVR is skewed (Figure 2) and UroCuff quadrant is an ordinal variable. IPSS = International Prostate Symptom Score; Qmax = maximum flow rate; VV = voided volume; PVR = post-void residual volume; Pcuff = urine flow interruption pressure; FRE = flow rate efficiency

TABLE 3. **Univariable linear regression models of IPSS**

Model	Variable	Coefficient estimate	Standard error	p value	Adjusted R2
Age (years)	Constant	14.692	1.343	< 0.001	0.004
	Age	-0.044	0.020	0.030	
Qmax (mL/s)	Constant	12.818	0.334	< 0.001	0.014
	Qmax	-0.074	0.018	< 0.001	
Voided volume (mL)	Constant	14.148	0.457	< 0.001	0.030
	Voided volume	-0.007	0.001	< 0.001	
PVR (mL)	Constant	11.044	0.313	< 0.001	0.010
	PVR	0.006	0.002	0.001	
UroCuff Quadrant	Constant	9.105	0.565	< 0.001	0.024
	UroCuff quadrant	1.261	0.242	< 0.001	

Linear regression models of continuous IPSS values were fit individually for each variable. Each model in had one outcome variable, IPSS, and one predictor variable. IPSS = International Prostate Symptom Score; Qmax = maximum flow rate; PVR = post-void residual volume.

TABLE 4. **Multivariable linear regression model by PCT quadrants**

Covariate	Coefficient	Standard error	p value	95% confidence interval	Adjusted R^2
		Unobstructed			
Constant	12.269	0.843	< 0.001	(10.609, 13.929)	0.061
Age > 67	-2.170	0.794	0.007	(-3.732, -0.607)	
VV > 305	-2.835	0.817	0.001	(-4.442, -1.227)	
PVR > 78	2.028	0.778	0.010	(0.497, 3.559)	
		High pressure/high flow (HP/HF)			
Constant	12.616	0.767	< 0.001	(11.109, 14.123)	0.022
Age > 67	-1.520	0.715	0.034	(-2.925, -0.115)	
VV > 305	-1.775	0.739	0.017	(-3.227, -0.323)	
PVR > 78	1.272	0.709	0.074	(-0.123, 2.667)	
		Obstructed			
Constant	14.678	1.028	< 0.001	(12.656, 16.701)	0.015
Age > 67	-2.216	0.916	0.016	(-4.019, -0.413)	
VV > 305	-1.404	0.993	0.159	(-3.359, 0.551)	
PVR > 78	0.588	0.960	0.540	(-1.300, 2.477)	
		Low pressure/low flow (LP/LF)			
Constant	12.986	1.749	< 0.001	(9.504, 16.467)	-0.028
Age > 67	0.356	1.818	0.845	(-3.263, 3.975)	
VV > 305	-2.094	2.650	0.432	(-7.368, 3.181)	
PVR > 78	0.365	1.760	0.836	(-3.138, 3.869)	

Multivariable linear regression models of continuous IPSS were fit separately for each UroCuff quadrant. The predictor variables included in the models were binary indicator variables for age, VV, and PVR.
The binary indicator variables for age, VV, and PVR were determined using the sample median. For example, if a subject had an age greater than the sample median of 67, they were considered having high age.
VV = voided volume; PVR = post-void resideual volume; IPSS = International Prostate Symptom Score

78 mL was associated with a 2.0-point increase in IPSS (p = 0.010).

As patients progress through the bladder life cycle, these relationships became weaker. For those in LP/LF quadrant, age, VV, and PVR are no longer significant predictors of IPSS. For example, our subpopulation included 54 patients who were in the LP/LF quadrant with PVR > 78 mL. Despite presenting with the most severe urodynamic voiding impairment, 14/54 (25.9%) of these patients reported a mild symptom score (IPSS ≤ 7), while only 12/54 (22.2%) reported a severe symptom score (IPSS ≥ 20).

Discussion

There is a significant body of literature comparing patient-reported symptom scores to objective voiding parameters.[1-5,16] Most often, the IPSS survey is used to compare to uroflowmetry or to catheterized urodynamic measurements. Almost universally, these studies have shown a weak correlation between these subjective and objective measures.

This is a large study with 1077 patients and is the first published comparison of IPSS and UroCuff PFS data. We demonstrated statistically significant relationships between IPSS and voiding parameters. Specifically, as IPSS increased, Qmax and VV decreased, and PVR and UroCuff quadrant increased (all p < 0.001). These relationships between reported symptoms and deteriorating urodynamic function match our clinical intuition. However, the correlations between each of these voiding parameters and IPSS are weak. This indicates that while the relationships hold true for the large population, each patient may have additional factors that influence their IPSS score. One does not predict the other. Furthermore, our data showed that the correlation between IPSS and voiding parameters becomes weaker as voiding parameters deteriorate, and patients move from the unobstructed quadrant to the more impaired quadrants.

The low correlation between IPSS and voiding parameters has profound implications on optimizing a disease management strategy. For example, we observed that 12% of urodynamically unobstructed patients self-report severe symptoms and 25% of urodynamically obstructed patients self-report mild symptoms. The unobstructed patients with severe symptoms are unlikely to benefit from deobstructive procedures while the obstructed patients with mild symptoms risk bladder deterioration from extended watchful waiting. These findings reinforce the importance of following the AUA BPH guidelines, which may include additional evaluation steps such as urinalysis, PVR, and an assessment of prostate size and shape.

With regard to the relationship between IPSS and age, we observed that for the first three UroCuff quadrants (unobstructed, HP/HF and obstructed), age and IPSS are negatively correlated. For example, in the obstructed quadrant, patients > 67 years presented with IPSS 2.2 points lower than patients ≤ 67 years. This may reflect the "normalization" of self-reported symptoms that occurs in chronic suffers. Patients who experience a sustained duration symptoms may present as less subjectively bothered over time, even with sustained or worsening symptoms. This age associated normalization of symptoms may be an obstacle to our clinical goal as urologists to preserve bladder function through timely intervention.

Our findings support the historical findings of the urological community, and as concluded by Bosch et al in 1995, "The parameters used to characterize benign prostatic hyperplasia should be considered independently because no predictions about the value of a certain parameter can be made by knowing one of the other parameter values. Symptom scores should therefore not be used as a pre-selection criterion in the determination of the prevalence of clinical BPH without taking other measures into account."[1]

Conclusions

For optimal patient care, it is crucial that both symptom scores and voiding profiles are compared and analyzed. The combination of these two data sets paints the clinical vignette and gives valuable insights as to care pathways that help the patient to effectively store and empty, as well as experience minimal symptoms. □

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