The UroCuff Test: a non-invasive alternative to pressure flow studies in adult males with lower urinary tract symptoms secondary to bladder outlet obstruction

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Introduction: *To assure that patients with lower urinary tract symptoms (LUTS) benefit from interventions, urologists must practice careful selection of surgical candidates. Currently, 15%-30% of men do not benefit optimally from these invasive and potentially morbid procedures. Success rates following transurethral resection of the prostate (TURP) are higher if bladder outlet obstruction (BOO) is confirmed prior to the procedure by invasive pressure flow studies (PFS). However, PFS may not be performed because of many reasons. We report a study of a non-invasive method of assessing BOO.*

Materials and methods: *The UroCuff test was compared to invasive urodynamic studies in adult males with lower urinary tract symptoms. Patients undergoing PFS for LUTS presumed to be due to BOO were recruited from a single site to perform a penile cuff test (UroCuff) at the same time as PFS. Standard PFS were performed followed immediately by a penile cuff test in the same test setting. The results were compared using basic statistical analysis.*

Results: *A total of 19 men were evaluated by both PFS and UroCuff evaluation. Using PFS as the gold standard, the positive predictive value of the UroCuff penile cuff test to diagnose BOO was found to be 92%. The sensitivity of the UroCuff test for detecting BOO was 75%. When compared to PFS, patients preferred the UroCuff 100% of the time.*

Conclusions: *The UroCuff test is accurate in predicting BOO when compared to conventional invasive pressure flow studies in men with LUTS. It is well tolerated and preferred over invasive pressure flow studies.*

Key Words: urodynamics, prostatic hyperplasia, bladder neck obstruction, bladder outlet obstruction, lower urinary tract symptoms

Introduction

Male patients commonly seek urologic care for relief of their lower urinary tract symptoms (LUTS). Roughly 20,000,000 men nationwide are affected by these symptoms and benign prostatic hyperplasia (BPH) is very frequently the etiology. However, these symptoms can be caused by other urologic conditions like bladder cancer or benign disease such as detrusor hypocontractility (DH) or detrusor overactivity (DO).

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The International Continence Society (ICS) recommends quantitative symptom scoring using the IPSS questionnaire as the minimum evaluation prior to therapy for LUTS. Other forms of non-invasive testing include urine flow rate and post void residual. However, these tests have their limitations when determining whether or not a patient would benefit from surgical intervention.[1,2] Several studies have shown that the key to appropriately treating patients' LUTS is properly differentiating the etiology of the symptoms.[3-8] It is widely accepted that, heretofore, the only absolute method of accurately distinguishing bladder outlet obstruction (BOO) as a distinct cause of low urinary flow rate (and/or elevated post void residual) in men is by means of invasive pressure flow studies (PFS).

PFS are not routinely performed on all men prior to surgical treatment due to the potential for patient

discomfort, infection risk, and cost associated with skilled staff and specialized equipment. This is despite the fact that men with diagnosed BOO from PFS may have success rates 15%-29% higher than those without.[9]

Seeking a less invasive, simpler and cheaper alternative to invasive PFS, a completely non-invasive test, the CT3000, commercially known as the UroCuff (SRS Medical, Feeding Hills, MA, USA), was created. Already, the UroCuff system has been demonstrated to be easy to perform, rapidly diagnostic, inexpensive, and preferred over invasive urodynamics by 80% of patients.[10] Briefly, The CT3000 is a noninvasive bladder pressure measurement using controlled inflation of a flexible cuff placed around the penis during voiding until flow is interrupted in a manner analogous to systolic blood pressure measurement by a sphygmomanometer. Cuff pressure at flow interruption theoretically reflects isovolumetric intravesical pressure, a measure of detrusor contractility. An estimate of isovolumetric bladder pressure and a measurement of maximum flow rate are obtained and plotted on a modified ICS nomogram to allow categorization into obstructed, not obstructed, or "diagnosis uncertain" groups. Notably, isovolumetric bladder pressure, an important diagnostic parameter, is currently only measured by invasive techniques.

The CT3000 system cuff is automatically inflated during the voiding process to stop urine flow, and then deflated again. The inflation/deflation cycle is repeated several times during a single emptying of the bladder and from this the cuff pressure needed to stop the flow of urine is determined. This provides a measure of the fluid pressure generated in the bladder which is used to diagnose voiding problems associated with BOO and to distinguish BOO from problems associated with a DH or DO.

Eighty-nine percent of patients diagnosed as having BOO by the UroCuff were confirmed by gold standard PFS to have BOO.[11] Also, when using non-invasive pressure measurements in surgical decision making, a high proportion (87%) of patients had a good outcome from transurethral resection.[4,12] This ability to predict the success of surgical intervention is reported to be equivalent to that offered by invasive urodynamic studies.[4,5]

Two clinical trials (150 and 179 patients, respectively) have already shown that the degree of accuracy offered by the non-invasive pressure measurements is greater than the accuracy achieved by flow rate measurement and symptomatic assessment.[4,13]

As such, the UroCuff system shows significant potential for use in outpatient urology clinics. Such use may reduce the proportion of ineffective surgical interventions and also reduce, but not eliminate, the requirement for invasive urodynamic studies. To our knowledge, our study represents the first prospective look at the ability to diagnose obstruction using the UroCuff test in self-matched patients during evaluation for LUTS.

Materials and methods

Subjects

After obtaining IRB approval, 37 consecutive men presenting with LUTS such as hesitancy, poor flow, straining, intermittency, terminal dribbling and/or incomplete emptying between the ages of 18 and 89 were recruited from a single institution over an 8 month period between June 2011 and January 2012. Patients with prior recent (1 week) start of alpha-blocker or 5-alpha reductase inhibitor, prior history of prostatectomy, TURP or other surgeries to treat LUTS, or untreated symptomatic urinary tract infection within 1 week of study procedure were excluded prior to the study.

Experimental protocol

After informed consent, a medical exam to collect a history and physical was conducted. The subject then underwent catheter based urodynamics followed by the study device (UroCuff). Both tests were performed standing. After both procedures were conducted consecutively, during the same visit, the subject had completed his participation in the trial. The primary endpoint in the study was to validate the CT3000 UroCuff test as a diagnostic tool for BOO when compared to catheter based PFS in men with LUTS. Subjects acted as their own control. The secondary endpoint was subject satisfaction with the CT3000 UroCuff versus catheterized PFS.

PFS test protocol

In the standard fashion, following local anesthetic gel instillation, a 7Fr duel transducer air-charged cystometry catheter was inserted into the bladder under aseptic conditions and a 9Fr air-charged manometer catheter was inserted into the rectum. The air-charged lines were connected to external pressure transducers, zeroed to atmospheric pressure according to standard urodynamic practice. The bladder was filled with room temperature 0.9% saline and infused at a rate of 50 mL per minute with the subject standing. At cystometric capacity, recognized by the subject indicating a strong desire to void, filling was stopped and the subject was asked to void. Intravesical

pressure (Pves), abdominal pressure (Pabd), subtracted detrusor pressure and flow rate were continuously recorded at a sampling frequency of 10 Hz.

A the conclusion of the PFS test the bladder was re-filled with room temperature 0.9% saline and infused at a rate of 50 mL per minute to a volume at, near the previously identified maximum volume. The catheters and manometer lines were then removed.

Cuff test protocol

With the subject standing and the bladder previously filled, the cuff was applied to the penis and the height difference between the upper border of the symphysis pubis and the middle of the cuff was recorded. The CT3000 UroCuff procedure was then initiated and the subject was asked to void.

Peri-procedural exclusion criteria included no flow recovery after cuff deflation (indicative of the void finishing sometime during the current inflation cycle and/or that the cuff may not be responsible for stopping the flow), an erratic flow trace, leading to ambiguity about the cuff pressure at flow interruption, flow uninterrupted at the instrument's maximum pressure of 200 cm H_2O, or total void (V_{void}) < 150mL.

Test preference assessment

A single question was asked of each patient at the conclusion of the study protocol to assess their experience with the PFS and combined CT300 UroCuff Test. The question was asked verbally: "When thinking about the PFS and the CT3000 UroCuff test, please pick the most appropriate answer: 1) I prefer the cuff test, 2) I have no preference in testing, 3) I prefer the invasive PFS."

Statistical analysis

Basic statistical analysis was completed comparing the UroCuff prediction of obstructed or equivocal versus unobstructed to the gold standard pressure flow studies numerical based diagnosis. Positive and negative predictive value, specificity, sensitivity were noted. For the purposes of analysis, the obstructed and equivocal diagnoses for each study were grouped together and separated from unobstructed. In addition, the correlation of maximum urine flow rates reported for each study was determined using Spearman's rank correlation coefficient.

Results

A total of 37 consecutive men seeking treatment for LUTS were enrolled into the study to be evaluated by both PFS and UroCuff evaluation. Twelve men failed peri-procedure screening as described in the protocol.

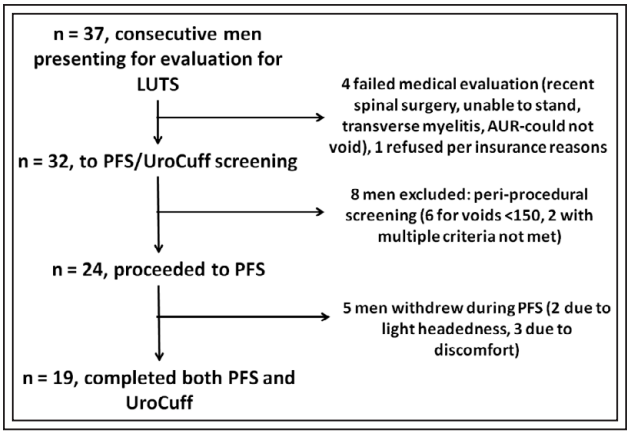

Figure 1. Thirty-seven consecutive patients were evaluated with 19 patients meeting all inclusion/exclusion criteria and eventually completing all necessary tasks for complete study involvement.

Of these criteria, six men were excluded only for failure to void more than 150 mL of urine, and two were excluded for a combination of failure to void 150 mL as well as at least one other criterion. Four addition men were excluded for the following reasons: unable to stand to complete study, history of transverse myelitis, recent spinal surgery, and insurance reimbursement prohibiting study. Six men withdrew; 4 without reason given and 2 because they got light headed during PFS with spontaneous resolution of symptoms with no requirement of medical intervention, Figure 1. No patients withdrew for adverse events that occurred during UroCuff study. Nineteen men are included in the data set. Mean IPSS was 16 (6-30) with mean QoL subscore of 3.4. Using PFS as the gold standard, the sensitivity of the UroCuff test for detecting BOO was 75% while the specificity was 66%. The positive predictive value of the UroCuff penile cuff test to diagnose BOO was found to be 92%. The test was preferred to invasive pressure flow monitoring in 100% of subjects and no adverse events were reported.

Figure 2 displays each of the 19 patients cuff pressure plotted against flow rate on a modified ICS nomogram. This nomogram was validated internally by the proprietary company with a 143 patient study. The position of the plot on the figure represents the UroCuff findings of each patient while the shape of the plotted patient represents their diagnosis based on PFS. Positive corroboration between the two tests can be seen when the obstructed or equivocal (triangle and square, respectively) is plotted above the cut off line or when the unobstructed patient (diamond shape) is plotted below the line.

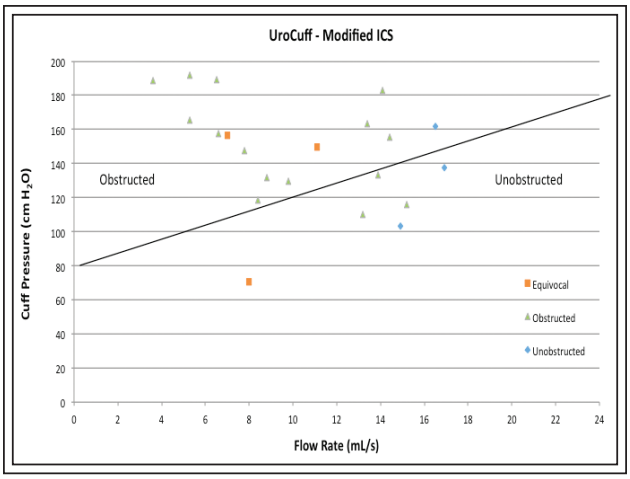

Figure 2. The Modified International Continence Society (ICS) nomogram specifically for the UroCuff test. The position on the graph represents the UroCuff findings of each patient while the shape of the plotted patient represents their diagnosis based on pressure flow studies.

When the maximum urine flow rates were examined from each test, they were strongly correlated with a Spearman's rho = 0.76 (p = < .0002), as per Figure 3. Detrusor pressure and cuff pressure at the time of occlusion of urine flow were correlated with a Spearman's rho = 0.54 (p = 0.02), as per Figure 4.

Discussion

For many years, it was presumed that the cause of LUTS in most men of age was BOO. Our further understanding of bladder function and its relationship to the outlet over the last decade or so has elucidated

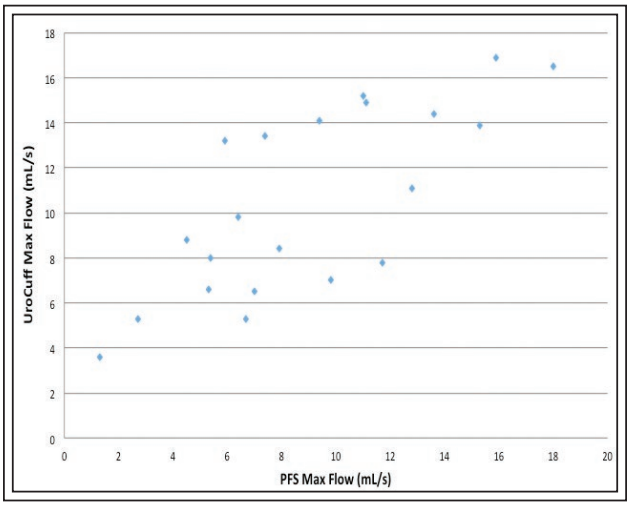

Figure 3. Correlation of pressure flow maximum flow rate and UroCuff maximum flow rate.

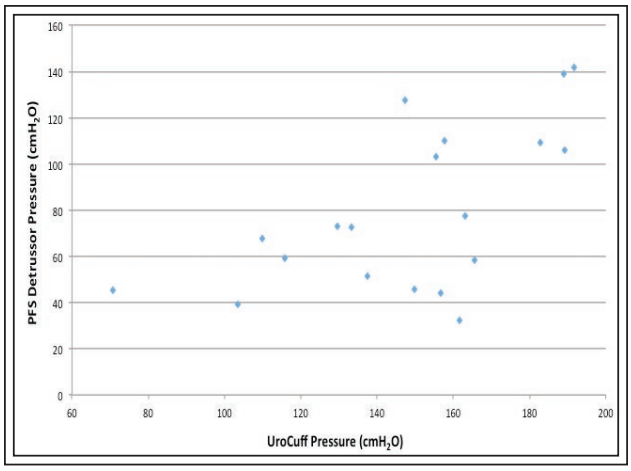

Figure 4. Correlation of detrusor pressures from pressure flow studies and UroCuff maximum cuff pressure that lead to cessation of urine flow.

the difficulties in determining whether or not a man requires or would benefit from surgical therapy for his symptoms. There is an increased appreciation that DO frequently coexists with BOO, and in many cases may be the sole cause of the patient's LUTS. In addition, detrusor hypocontractility (or in the future, one might hear the term detrusor under activity) is also being recognized as likely an underreported entity, particularly with aging.[6] The population continues to live longer and the prevalence of BPH is also a linear function known to be an almost inevitable consequence of advanced age. With a constellation of symptoms as common and prevalent as LUTS and an aging population, the accurate diagnosis of the basic etiology of the symptoms could potentially save an immense amount of time, money, and potentially morbid sequelae.

Although both American and European guidelines stop short of recommending invasive urodynamics routinely for the evaluation of LUTS in men[1,2] current evaluation with symptom questionnaires do not correlate very well with the presence or absence of BOO.[14] Use of post void residual and urine flow rates are recommended as adjuncts in those patients in whom BOO is suspected. However, these do not easily discriminate between BOO and detrusor hypocontractility. Thus, once attempts at conservative management medical management of the presumed etiology has failed, and one is contemplating more invasive therapy, it would seem that making a proper diagnosis of BOO is of the utmost importance.[3,5-7]

The only currently accepted gold standard to definitively make the diagnosis of BOO is by means of invasive PFS. In addition to being potentially uncomfortable, these can be costly and time consuming in

the clinical setting. Furthermore, as delivery of healthcare evolves, economic constraints will dictate that technology produce cost-effective and accurate tests to determine who will benefit from costly surgical procedures and who could potentially fail treatment. All of these factors have created a tendency to skip this conclusive diagnostic measure and proceed directly towards invasive surgery, which is potentially partially ineffective if performed on a patient in the absence of BOO.

Non-invasive bladder pressure measurement has already been proven in the literature in multiple studies to be a relatively accurate assessment of isovolumetric bladder pressure. Further refinement of the procedure and analysis led to the development of the UroCuff test. Previous studies have shown penile cuff testing to be a good predictor of surgical outcome with 87% of patients diagnosed with obstruction found to have a successful outcome versus 56% without obstruction.[4] This was validated in a more recent study, where 94% of patients achieved a good outcome following surgery when found to be obstructed on penile cuff testing versus 70% who were unobstructed on testing.[12] To our knowledge, our study is the first study using subjects as their own control to show a positive predictive value of 92% on the UroCuff CT3000 when compared to PFS. This suggests that few patients will be improperly diagnosed with obstruction by the UroCuff test and provides increasingly confirmatory data in the setting of previous published studies on non-invasive pressure testing. Data supports a fast learning curve and agreement amongst "experts" and novices after a short training period.[15]

When comparing the UroCuff and PFS, the maximum urine flow rates and pressures recorded by each method showed strong correlation, Figures 3 and 4. This is of interest given the difference in method used to record it-- flow interruption versus continuous flow and the fact that flow rate is the simplest form of non-invasive urodynamic measurement. Internal validation data from 143 patients performed by the company supports even greater sensitivity and specificity for obstruction when combining the nomogram diagnosis and the flow data's (Qmax < 10mL/s) agreement.

There are some potential pitfalls with the any non-invasive pressure measurement method. It is inherently impossible to use in the setting of acute urinary retention (AUR) and is, theoretically untested in patients who have such severe LUTS that they cannot void other than in small volumes, although invasive PFS can likewise be difficult to interpret in the latter setting. There are similar penile cuff prototypes being developed which assess "almost-zero" flow with a continuous measurement which could potentially help eliminate this issue.[16] In settings where PFS are refused by the patient, the UroCuff test has its greatest benefit over PFS as it will provide additional diagnostic information in a situation where it otherwise would not be possible.

Of the patients who were excluded by peri-procedural screening criteria (n = 8) in our study, the majority were excluded due to low voided volume. Of these patients, most actually achieved an adequate voided volume for the PFS, but not upon refilling for the UroCuff, an obvious artifact of the study design. One would expect that under different circumstances (that which would be encountered in clinical practice), they would have been able to achieve an adequate voided volume. Further, the principle that urethral compression is always equal to pressure during isovolumetric contractions of the bladder does not address the possibility of concomitant stricture impeding flow between the bladder and the cuff. As with other forms of non-invasive bladder pressure measurement, the lack of concomitant intra-abdominal pressure measurement limits its ability to evaluate for Valsalva voiding. Non-invasive testing also does not assess the storage phase, which can be particularly important in patients with severe LUTS. Thus, the contribution and effect of any OAB component on measurement of BOO is not well-described, furthermore, bladder compliance cannot be evaluated. For these reasons, non-invasive measurements should not replace invasive PFS for patients in whom these variables need assessment or in whom the non-invasive test is inconclusive.

Conclusions

Non-invasive evaluation using the CT3000 UroCuff penile cuff test is accurate in predicting BOO when compared to conventional invasive pressure flow studies in men with LUTS. In addition, the test is well-tolerated and clearly preferred by patients over invasive PFS by patients. These confirmatory findings represent the first comparison between the UroCuff CT 3000 and invasive pressure flow studies in the same patient at the same setting. Non-invasive penile cuff test may be seen as an attractive alternative to invasive PFS when evaluating a patient's suitability for outlet procedures secondary to presumed BOO. The test is quick and easier to perform than invasive urodynamics which should aid in more widespread clinical acceptance of this diagnostic modality.

Disclosure

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