

## **How can we maximise the diagnostic utility of uroflow? : ICI-RS 2017**

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Abstract: Intro, Methods, Results, Conclusions

### **Introduction**

The assessment of urine flow rate dates back to the 1950's and uroflowmetry is to date the most widely-used urodynamic assessment. This is in part due to its non-invasive nature, practical simplicity and low cost. The test is recommended as an initial objective evaluation for patients with signs and symptoms of lower urinary tract dysfunction by the UK National Institute for Health and Care Excellence (NICE)<sup>1</sup>, European Association of Urology (EAU)<sup>2</sup>, International Consultation on Incontinence (ICI)<sup>3</sup> and American Urological Association (AUA)<sup>4</sup>. Although the recommendation for uroflowmetry is relatively undisputed, the evidence with regard to the predictive value of the test is not very well established. Moreover, much of the potential information that a flowrate measurement contains is not very well studied and the evidence about the most studied parameter, maximum flowrate ( $Q_{max}$ ), is not unambiguous. There is for example discrepancy in practice guidelines regarding recommendations for the use of specific cut-off values for  $Q_{max}$  in the assessment of men with lower urinary tract symptoms (LUTS). In a systematic review published recently only 30 studies could be included from a literature search dating back to 1970, confirming a dearth of high-level evidence regarding the diagnostic value of uroflowmetry<sup>5</sup>. The specific aim of this 2017 International Consultation on Incontinence Research Society (ICI-RS) think tank was to explore the question "How can we maximise the diagnostic utility of uroflow?". The areas of current knowledge are discussed with summaries of gaps in that knowledge. Recommendations are then made for studies to address those gaps.

### **Maximum flow rates**

One of the main problems with uroflowmetry is lack of diagnostic specificity associated with the test. The majority of existing work has centred on the ability of urine flow tests to provide an estimation of the likelihood of bladder outflow obstruction (BOO) in male patients. Outflow diameter (flow controlling zone) is directly related to flow rate, but also depends on intravesical pressure, and the parameter that has been most researched is maximum urine flowrate ( $Q_{max}$ ). The EAU LUTS guidelines comment that "The diagnostic accuracy of uroflowmetry for detecting BOO varies considerably, and is substantially influenced by threshold values"<sup>2</sup>. The evidence for this statement comes from large scale studies such as the ICS BPH study<sup>6</sup>. The study comprised 1271 men aged between 45 and 88 years recruited from 12 centres in Europe, Australia, Canada, Taiwan and Japan. They reported that a threshold  $Q_{max}$  of 10 mL/s has a specificity of 70%, a PPV of 70% and a sensitivity of 47% for BOO as defined by invasive urodynamics. Using a higher threshold for  $Q_{max}$  of 15 mL/s, the specificity was reduced to 38%, the PPV to 67% and the sensitivity increased to 82%. Thus, as in all diagnostic tests, there is a trade-off between sensitivity and specificity as different (flow rate in this case) thresholds are considered. Lower  $Q_{max}$  thresholds are more specific to diagnose BOO but less sensitive and as the threshold is raised the sensitivity increases but specificity decreases.

In women the relevance of maximum flowrate as a cut off is even more difficult to establish. The prevalence of female BOO is much lower than in males, but may nowadays be increasing, perhaps because of more interventions that can cause outflow obstruction<sup>7,8</sup>. Though for most women, flow rates are high (above 15 – 20 mL/s)<sup>9</sup>, the specificity of a low maximum flow rate towards the cause of dysfunction is not fully reported in the literature. Another group not extensively studied is healthy young men, who void with generally lower maximum flow rates than their female counterparts, which was observed especially when the voided volume is relatively low<sup>10</sup>. For women and for younger men, and to a lesser extent elderly men, therefore, very little conclusion can be drawn from uroflowmetry alone. As a starting point, volume correction for interpretation of the maximum flow rate is recently published.<sup>11</sup>

It is well known that maximum flow rate alone is insufficient for a specific diagnosis of LUT function, but there is not yet much evidence that other signs and symptoms, apart from age and gender, can be combined with this measurement to enhance diagnostic power.

### **Multiple uroflow measurements**

Uroflowmetry is a clinical test that is performed by the patient. Inevitably, within-patient variability of the measurements made plays a role in the result. The AUA have noted in their recent guideline that “Clinicians should be aware that uroflow studies can be affected by the volume voided and the circumstances of the test” and advise that “Serial uroflowmetry measurements which are consistent, similar and comparable provide the most valuable information for the clinician.”<sup>4</sup> This has led to a general recommendation that uroflowmetry parameters should preferably be evaluated with voided volume >150 mL and that serial measurements are most informative. This is supported by a study from Reynard et al. who concluded that the maximum  $Q_{\max}$  of three clinic flow measurements provides a valuable improvement in diagnostic power over a single measurement to estimate the likelihood of BOO in elderly males with prostate enlargement<sup>12</sup>.

A logical follow-on from these data has been the development of home uroflowmetry devices which can capture multiple voids under “usual” circumstances and thus theoretically reduce single observation inaccuracy. In a systematic review on the subject of home uroflowmetry recently published it was concluded that “the statistical benefit of averaging multiple measurements of  $Q_{\max}$ , made feasible by home uroflowmetry, should translate to improved diagnostic accuracy and assessment of treatment outcome”<sup>13</sup>. However at the moment further studies are necessary to confirm this benefit, particularly to examine both the diagnostic and predictive value of flow variables derived from multiple recordings.

### **Flow-volume nomograms**

Nomograms that allow for correction of flow rate for either the volume voided or the volume in the bladder are frequently presented and are produced from all urodynamic equipment. However, the utility of these for diagnosis varies greatly and is never strong. These nomograms are unable to provide a urodynamic diagnosis but can indicate the probability of normality of maximum flow rate. The premise that inter-patient volume correction with these nomograms helps to establish better evaluation of treatment effect (on  $Q_{\max}$ ) has not been confirmed.

Siroky<sup>14</sup> produced a flow-volume nomogram from 80 male patients of unreported age, with bladder volume (not voided volume) on the vertical axis. Later, Kadow<sup>15</sup> selected 123 older (between 50 and 80 years) male patients, and formed a nomogram with slower flow rates than Siroky, but using voided volume alone. The most comprehensive set of nomograms came from Haylen’s Liverpool study<sup>16</sup>, which produced nomograms from 331 male and 249 female patients of a wide age range. The Liverpool nomograms include, as did Siroky, graphs for both maximum and average flow rates, but also included a factor for age in the male equations and used voided volume. More recently, male<sup>17</sup> (bladder volume) and female<sup>18</sup> (voided volume) ‘PGIMER’ nomograms have been proposed for Indian populations, with factoring for the age of female patients. Additional proposals for male assessment have been made for individualised nomograms based on multiple flows<sup>19</sup> and the D index from within the VBN modelling system<sup>20</sup>.

The clinical perspective is that flow rate is a screening test and that normal flow rate can be used to exclude voiding abnormalities. Since the nomograms are all proposed for indicative, rather than diagnostic, use, they are limited in application to initial screening and indication of treatment outcome. Nevertheless the sensitivity, specificity, type of volume measured and influence of age and population type for each nomogram could be more clearly described and understood, otherwise unmerited diagnostic capacity may be assumed.

### **Flow rate curve shape**

The terms used to describe the shape of the urine flow rate curve over time vary considerably. In paediatric urology the analysis of uroflow pattern is standardized to a certain extent<sup>21</sup>, although anomalies exist, and shape can serve as a guide to the existence of a specific condition<sup>3,21,22</sup>. Since

patient inhibition can occur during uroflowmetry, good technical performance of the test is critical, or dysfunction may be erroneously diagnosed on the basis of procedure faults or technical artefacts.

Some of the terms to describe abnormally shaped flow curves may be regarded as confusing. For instance 'staccato-shaped' is used to describe an irregular, fluctuating curve and 'interrupted-shaped' to describe a curve with segments with zero flow<sup>21</sup>, yet 'staccato' truly means 'separated, detached'. Standard descriptions of uroflow curve in adults have other difficulties, for instance the descriptions 'constrictive' and 'compressive' are used for different uroflow shapes<sup>23</sup>. Those labels are, however, describing the cause of the shape rather than the shapes themselves. Consistency and clarity in description is therefore required, in order that a full analysis of the diagnostic utility of uroflow shape can be undertaken.

Two research teams have used  $Q_{\max}$  and  $Q_{\text{ave}}$  to diagnose urodynamic abnormality, and suggest relevance and applicability.<sup>24,25</sup> However the accuracy varies when trialled on different databases and the limitations have been discussed<sup>26</sup>. A recent study<sup>27</sup> has presented some mathematical analysis of uroflow curve shape, counting multiple peaks within filtered curves and considering the frequency content of the curve shape, but this has so far analysed only small numbers of patients and the specificity does not yet exceed that of the simple  $Q_{\max}$  cut-off of 10 ml/s to select symptomatic men with a high likelihood of BOO.

The current definition of dysfunctional voiding<sup>22</sup> is confusing, referring as it does to irregular flowrate caused by inability to void and or by underactivity of the detrusor and / or by outlet smooth or striated muscle activity. A container term as this is not helpful to ensure either optimum management or research to improve treatment for voiding difficulties.

### **Uroflow time measurements**

ICS GUP defines flow time as "the time over which measurable flow actually occurs"<sup>23</sup>. However, the threshold above which flow is considered "measurable" is not defined, and the equipment sensitivity will therefore affect the time value recorded. The end of micturition is presumably considered to be at the end of measurable flow, but most urodynamic pressure flow studies will end with the patient giving a final cough, possibly resulting in measurable leakage which should not be regarded as part of the normal void. A recent study proposed that 0.5 ml/s be used as the standard threshold for registering flow and that post-void leaks be ignored for the purpose of time recording<sup>28</sup>. Rollema<sup>29</sup> reported that diagnosis of bladder outflow obstruction in men could be improved by considering the time from  $Q_{\max}$  to the point where 95% of voided volume had been voided, but this parameter has never been confirmed and has not become standard.

### **Other measurements alongside uroflow**

Flow lag time, defined as the time between pelvic muscle EMG decrease and urine flow beginning has been reported either to increase or to decrease as an effect of management of a variety of dysfunctional voiding types in children.<sup>30</sup> However, standardisation of meatus to flowmeter distance (or of intravesical or voided volume) has not been carried out in these studies. Pelvic floor dysfunction as a cause for irregular voiding can be expected to be present in adults, although the evidence, e.g. from studies that report pelvic muscle EMG, is lacking<sup>3</sup>.

Given that abdominal straining has variable effects on flow rate, it is reasonable to suggest that non-invasive synchronous recording of abdominal pressure be investigated in different groups of patients. One study found that patients with detrusor underactivity are more likely to strain on voiding<sup>31</sup>, while another found that men with bladder outlet obstruction strained less<sup>32</sup> which is understandable since a prostate receives just as much pressure increment as the bladder, as a consequence of its intraabdominal position, during abdominal pressure rises.

### **Areas for research**

In view of the gaps in current knowledge detailed above, we recommend that studies be carried out to address the following research questions:

- Can maximum flow rate be improved as a diagnostic criterion for adult women and young adult men?
- Which definition of voiding dysfunction would be best applicable in clinical practice?
- What signs and symptoms can be combined with uroflowmetry to enhance its diagnostic power?
- Should an adult EMG – uroflowmetry test be designed?
- Should an abdominal pressure – uroflowmetry test be designed?
- How can the normalisation of flow rate to volume be improved, and nomograms consequently standardised?
- How can urine flow curve shape analysis be standardized and quantified?
- How can multiple flows and home uroflowmetry be applied to increase diagnostic accuracy?
- How can thresholds and protocols for measuring urine flow time be more clearly defined?

### **Conclusions**

The ICI-RS 2017 meeting has proposed a number of research questions that should be addressed to increase the diagnostic utility of non-invasive uroflowmetry. There is scope for combining uroflowmetry with other non-invasive indicators, and for better standardisation of the test technique, flow-volume nomograms, uroflow shape descriptions and time measurements. Given the ubiquity of the test, and its vulnerability to misunderstanding, there is a need for a consensus document on Good Practice for Uroflowmetry.

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