Percent Post-Void Residual over Bladder Capacity has the Strongest Correlation to the Highest White Matter Tracts in Women with Multiple Sclerosis and Voiding Dysfunction

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ABSTRACT

Multiple Sclerosis can lead to bladder storage and or voiding dysfunction. However, voiding dysfunction has been difficult to reliably quantify and track in MS patients. Here, we present an analysis that assesses the reliability of utilizing % post-void residual/bladder capacity as a strong correlate with both the Expanded Disability Status Scale (EDSS) and white matter integrity. Our cohort included 10 adult women with clinically stable MS and voiding dysfunction. We utilized the DTI 81 atlas to analyze white matter tract integrity and Pearson's correlation analysis to assess association. Overall, we found that %PVR/BC, among other parameters such as uroflow PVR, flow time, and MS Duration, can be utilized as an objective parameter in which to gauge voiding efficacy and response to therapy in MS patients.

BACKGROUND/METHODS

Multiple Sclerosis is an autoimmune inflammatory disease affecting white matter tracts and can lead to bladder storage and/or voiding dysfunction (VD). VD refers to abnormally slow and/or incomplete micturition, based on uncharacteristically slow urine flow rates and/or excessive post-void residuals (PVR) [1]. However, the absolute values of PVR of urine are unreliable metrics in the setting of MS where bladder capacity (BC) and compliance can also be decreased. The Expanded Disability Status Scale (EDSS) allows for quantification of disability in MS and for monitoring the changes in severity of disability over time; it is the most widely accepted measure for tracking disability progression in MS patients. We hypothesize that % post-void residual/bladder capacity (%PVR/BC) correlates strongly with both EDSS and changes in white matter integrity as seen on Diffusion Tensor Images (DTI).

- Ten adult women (>18 years of age) with clinically stable MS for > 3 months and D defined as %PVR/BC > 40% or Liverpool nomogram percentile less than 10th percentile were recruited for our tertiary Neuro-urology clinic.
- Patients participated in a clinical urodynamic study (UDS) and completed several questionnaires (i.e. Urogenital Distress Inventory (UDI-6), NBSS, AUASS).
- DTI Images were acquired using a 7-Tesla Siemens MAGNETOM Terra MRI scanner (Matrix = 158 x 158, slice thickness 1.4 mm, Field-of-View (FOV) = 220 x 220 cm^2, 64 directions, b-value = 1000 s/mm2, with a total scan time of 12 minutes and 14 seconds).
- DTI maps were constructed, and individual patients were co-registered with the ICMB-DTI-81 white atlas, which is a reference coordinate system containing the probabilistic locations of 50 white matter tracts, averaged from 81 different individuals.
- The Spearman's correlation test was performed between each WMT and clinical parameters both objective (uro-flow and UDS) and subjective (validated questionnaires).

Subjective:

1. UDI-6 (Urinary Distress Inventory)
2. HAM-A (Hamilton Anxiety Rating)
3. HAM-D (Hamilton Depression Rating)
4. AUASS (AUA Symptom Score)
5. HDAS (Hospital Anxiety and Depression Scale)
6. IIQ-7 (Incontinence Impact Questionnaire)
7. NBSS (Neurogenic Bladder Symptom Score)
8. EDSS (Expanded Disability Status Scale)

Objective:

1. Maximum Detrusor Pressure
2. Voided volume
3. Post-Void Residual
4. Maximum Cystometric Capacity (MCC)
5. PVR/MCC
6. Voiding Time
7. Flow Time
8. Maximum Velocity
9. Mean velocity
10. Nomogram Percentile

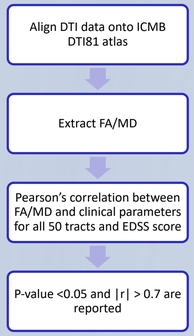

Figure 1. Subjective Clinical Parameters (left) and Objective Clinical Parameters (middle) used in correlation analysis. Overall data analysis workflow (right)

RESULTS

	Cohort Size (n = 10)
Gender	Female
Mean Age	53.4
Mean IIQ-7 score	10.4
Mean UDI-6 Score	11.6
Mean MS duration (years)	16.3

Table 1. Highlighted Cohort Characteristics

Parameter	%PVR/BC	Uroflow PVR	Flow time (s)	MS Duration (Years)	AUASS, Q3 (continuous stream)
Correlation Coefficient	0.551	0.478	-0.527	0.407	-0.407
P-value	.099	0.162	0.230	0.242	0.244

Table 2. Clinical Parameters with the Five Strongest Correlation to EDSS

- Key Cohort Characteristics are Listed in Table 1.
- Parameters with correlation to highest numbers of WMTs are shown in Table 2.
- Amongst these, %PVR/BC obtained from average of multiple un-instrumented uroflow assessments had significant correlations to the most amount of WMTs when assessing FA and MD.

Fractional Anisotropy (FA)	
Clinical Parameter	# of WMTs with Strong Correlation
HAM-D, %PVR/BC	8
AUASS-Q3 (intermittency)	7
Mean Diffusivity (MD)	
%PVR/BC	9
Voided Volume, Voiding Time	8
HAM-A, NBS QoL	6

Table 3. Clinical Parameters with Correlations to the Greatest WMTs

- Furthermore, we found that out of all clinical parameters analyzed, %PVR/BC had the strongest correlation with the EDSS score (Table 3), although none of these correlations were significant at an alpha of 0.05.

CONCLUSIONS

- %PVR/BC seems to be a suitable metric from which to monitor VD in women with MS where the bladder capacity can be variable and absolute value of PVR may not be reliable.
- However, an important limitation exists: We must confirm that the regions of the white matter skeleton that correlate to severity of VD in MS patients are localized to the same areas of the greatest white matter lesion burden.
- Results from this study demonstrate that %PVR/BC can be used as a reliable, objective parameter in which to gauge voiding efficacy and response to therapy in MS patients.

REFERENCES

1. Karmakar D, Sharma JB. Current concepts in voiding dysfunction and dysfunctional voiding: A review from a urogynaecologist's perspective [retracted in: J Midlife Health. 2018 Jan-Mar;9(1):50]. *J Midlife Health*. 2014;5(3):104-110. doi:10.4103/0976-7800.141185