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URINARY NERVE GROWTH FACTOR IS A BETTER BIOMARKER THAN DETRUSOR WALL THICKNESS FOR THE ASSESSMENT OF OVERACTIVE BLADDER WITH INCONTINENCE

Hypothesis / aims of study
Increased levels of nerve growth factor (NGF) have also been reported in the bladder tissue and urine of patients with sensory urgency and detrusor overactivity (DO). The level of NGF in urine could increase bladder sensation or cause DO through some undetermined pathways. It has been hypothesized that detrusor wall thickness (DWT) increases in patients with overactive bladder (OAB). The thickened bladder wall decreases in response to antimuscarinic treatment, and measurement of DWT might therefore be a useful biomarker for evaluation of disease progression and effectiveness of treatment for OAB. The aim of this study was to compare the differences in urinary NGF and DWT between patients with OAB and controls to evaluate their suitability as biomarkers in OAB.

Study design, materials and methods
A total of 81 patients including normal controls (n=28), patients with OAB dry (n=28) and patients with OAB wet (n=25) were enrolled in this study. All patients underwent trans-abdominal ultrasonography (TAUS) of the bladder using an 8.0 MHz transducer (GE, E8C probe, U.S.A.) and GE ultrasound equipment (Logic-Q P5/A5, U.S.A.). Each subject had both separate natural-filling and catheter-filling TAUS determinations of DWT. Urine NGF and DWT measurements were performed at full bladder and urge to void after natural-filling or catheter-filling during pressure flow study. DWT was measured by trans-abdominal ultrasound. Total bladder volume was calculated as voided volume plus postvoid residual. Urinary NGF levels were measured by ELISA according to previously reported methods. The total urinary NGF levels were normalized to the concentration of urinary creatinine (NGF/Cr level). NGF/Cr levels were compared among all subgroups and controls. These two parameters were compared among different symptomatic and urodynamic subgroups.

Results
After completion of natural-filling or catheter-filling, the total bladder volume was 1.37±0.33 (range 0.95 to 2.46) and 1.47±0.58 (range 0.69 to 2.61) times that after natural-filling by TAUS or after catheter-filling by infusion volume, respectively. DWT decreased rapidly from empty bladder to a bladder volume of 250ml and slowly to the maximal bladder volume. DWT was not significantly different among subgroups at 250ml bladder volume. The total NGF levels in urine samples from natural-filling were significantly greater than those from catheter-filling in the OAB wet (p= 0.019) or urodynamic DO subgroups (p= 0.019). Although patients with OAB wet had a significantly greater DWT at the maximal bladder volume, this difference was not significant from controls after correction of the volume factor. By contrast, urinary NGF levels were significantly increased in patients with OAB wet and those with urodynamic detrusor overactivity. However, elevated NGF levels in OAB wet were found only after natural-filling and not after catheter-filling.

Interpretation of results
This study demonstrated that although the DWT in patients with OAB wet at maximal bladder volume was significantly greater than in controls or patients with OAB dry, this difference was due to a smaller bladder capacity in patients with OAB wet. Although there were significant differences in DWT among these groups, the differences were small. The urinary NGF levels found in the OAB patients of this study are consistent with previous reports.

Concluding message
Patients with OAB wet and urodynamic DO had significantly greater urinary NGF levels than controls and patients with OAB dry or hypersensitive bladder. DWT at maximal bladder volume was greater in patients with OAB wet because these patients had a smaller bladder volume than controls. Urinary NGF level was superior to DWT as a biomarker for assessment of OAB wet or DO in this study. Urinary NGF should be measured from natural-filling and not catheter-filling urine.

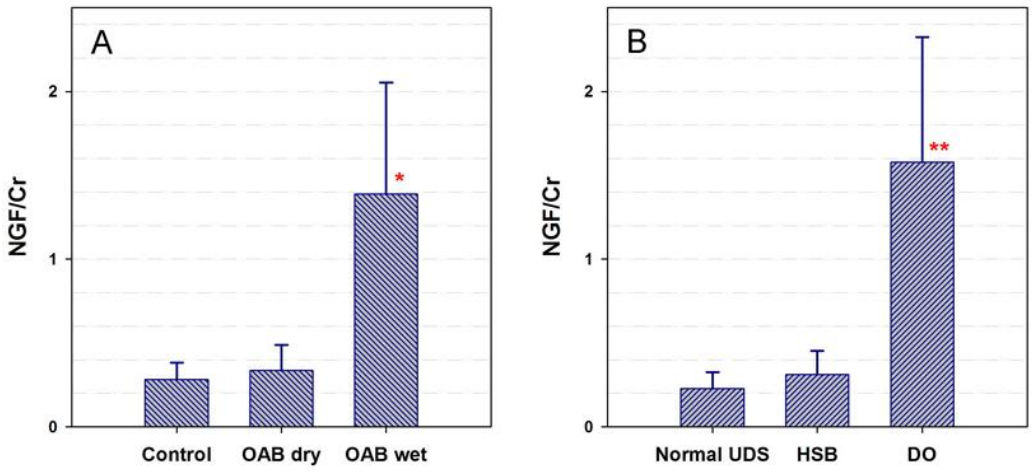

Fig. The urinary NGF/Cr levels in symptomatic and urodynamic subgroups. Asterisks represent significant difference among OAB wet or DO and other subgroups.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Institutional Review Board of Tzu Chi General Hospital and Tzu Chi University**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**