

Urinary TIMP-2 is significantly associated with poor bladder compliance and upper urinary tract damage in adult patients with spina bifida

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Peyronnet B.¹, Richard C.¹, Bendavid C.², Naudet F.³, Hascoet J.¹, Brochard C.⁴, Alimi Q.¹, Khene Z.¹, Siproudhis L.⁵, Bouguen G.⁶, Kerdraon J.⁷, Manunta A.¹, Gamé X.⁸

¹Rennes University Hospital, Dept. of Urology, Rennes, France, ²Rennes University Hospital, Dept. of Biochemistry, Rennes, France, ³University of Rennes, Inserm CIC, Rennes, France, ⁴Rennes University Hospital, Dept. of Gastroenterology, Rennes, France, ⁵Rennes University Hospital, Dept. of Gastroenterology, Rennes, France, ⁶Rennes university Hospital, Dept. of Gastroenterology, Rennes, France, ⁷Centre de Rééducation de Kerpape, Dept. of Rehabilitation, Ploemeur, France, ⁸Toulouse University Hospital, Dept. of Urology, Toulouse, France

Introduction & Objectives: The aim of the present study was to assess the predictive values of 5 urinary markers (NGF, BDNF, TIMP-2, TGF-B1 et PGE2) for detrusor overactivity/poor bladder compliance and for upper urinary tract damage in adult patients with spina bifida.

Materials & Methods: A single-center prospective trial was conducted from March 2015 to March 2017 including all consecutive adult spina bifida patients seen for urodynamic testing. The urine of the voiding/self-catheterization immediately preceding the urodynamic were collected and stored at -80°C. An upper urinary tract imaging was systematically performed. At the end of the inclusion period, urines were defrosted and urinary NGF, BDNF, TIMP-2, TGF-B1 were assessed using validated ELISA kits. The urinary markers level were adjusted on the urinary creatinine level. The primary endpoint was upper urinary tract damage defined as: renal scaring or renal atrophy or hydronephrosis on imaging.

Results: 41 patients were included. Of all urinary markers, only TIMP-2 was significantly associated with poor bladder compliance ($p=0.04$). There was no other statistically significant association between urinary markers and urodynamic parameters (bladder compliance, maximum detrusor pressure (Pdet max), maximum cystometric capacity or detrusor overactivity). TIMP-2 was also the only urinary marker significantly associated with upper urinary tract damage on imaging ($p=0.02$). Of all urodynamic parameters, poor bladder compliance was the only one associated with upper urinary tract damage ($p=0.01$), while Pdetmax did not reach statistical significance ($p=0.07$). The diagnostic performances of urinary TIMP-2 for upper urinary tract damage were slightly superior to PdetMax and slightly inferior to bladder compliance (ROC curves, figure 1) with an area under the curve (AUC) of 0.72. For the optimal threshold of 400 pg/ml, sensitivity was 71.4% and specificity was 74.1%.

Conclusions: This study confirms the potential interest of TIMP-2 to predict high-risk urodynamic features and upper urinary tract damage in adult spina bifida patients. This finding confirms the strong pathophysiological role of extracellular matrix alteration in adult spina bifida patients and DO/ poor bladder compliance. TIMP-2 could be a therapeutic target in this population.