



## Clinical diagnosis of bladder dysfunction in enuretic children and adolescents

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### Abstract

**Objectives:** To estimate the predictive value of diurnal voiding symptoms for the diagnosis of bladder dysfunction in enuretic children and teenagers receiving care at Fernandes Figueira Institute (Rio de Janeiro, Brazil).

**Methods:** From June 1999 to May 2002, 91 patients (aged 5-17 years) with enuresis, both monosymptomatic and polysymptomatic, were assessed based on medical history, voiding chart, physical examination, and urodynamic studies. The medical history was investigated for detection of diurnal voiding symptoms. The predictive value of these symptoms for the diagnosis of bladder dysfunction was estimated.

**Results:** Bladder dysfunction was observed in 94.5% of the children and teenagers with enuresis. Medical history identified 97.3% of patients with diurnal voiding symptoms. Increased discharge of urine was detected exclusively by voiding chart in only 2.7% of the patients. The positive predictive value of diurnal voiding symptoms for bladder dysfunction was 98.6%. There was a statistically significant association between diurnal voiding symptoms and bladder dysfunction ( $p < 0.005$ ). The risk for bladder dysfunction was approximately 20 times higher in presence of these symptoms.

**Conclusions:** The presence of diurnal voiding symptoms was a strong predictor of bladder dysfunction. Medical history was a useful instrument for detecting diurnal voiding symptoms and establishing the diagnosis of bladder dysfunction.

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### Introduction

The most often employed definition of enuresis is "involuntary urination at an age at which control should already have been achieved".<sup>1,2</sup> It is classified as nocturnal when involuntary urination occurs during sleep and diurnal when the child is awake.<sup>2-5</sup> The American Psychiatric Association's definition of enuretic covers children who are still wetting at five years or more.<sup>2</sup>

The International Children's Continence Society (ICCS)<sup>6</sup> defines enuresis as normal urination occurring at times or in places that are socially unacceptable.

Some children with nocturnal enuresis are quite able to control urination during the daytime. The term

monosymptomatic nocturnal enuresis has come to be employed to describe children with urinary behavior that is totally normal during the daytime, or when awake. Other patients also present diurnal urinary symptoms, such as: increased frequency of urination, incontinence, urge incontinence, maneuvers to prevent urine escape, an interrupted urinary flow and hesitation when starting to urinate. Such patients are classified as suffering from polysymptomatic enuresis. It is important that such clinical manifestations be investigated, even when there is no evidence of urinary incontinence, because of the possibility of voiding dysfunction.<sup>3,6-9</sup>

Voiding dysfunction occurs when one of the elements of the normal voiding process is affected, causing it to no longer function correctly. Thus abnormalities in the cortex, the brainstem, the spinal marrow, the detrusor or the sphincter complex may result in unsatisfactory

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urination, with inadequate urine storage and/or incomplete emptying of the bladder.<sup>10</sup>

Functional abnormalities of the lower urinary tract can be split into two groups: those that are caused by neurological abnormalities and those that are functional.

Voiding abnormalities caused by neurological alterations (neurogenic bladder) are most commonly the result of spinal dysraphisms (myelomeningocele, lipomeningocele, sacral agenesis and occult lesions) or cerebral palsy.<sup>10,11</sup>

Urinary dysfunction resulting from functional abnormalities occur with children in whom evidence of neurological disease is not found. They may present with the diurnal voiding dysfunctions listed above or with nocturnal dysfunctions, repeat urinary infections and vesicoureteral reflux. They often have intestinal constipation in association and soiling due to dysfunction of the pelvic floor also occurs frequently, in which case it is described as dysfunctional elimination syndrome.<sup>4,12,13</sup> An early diagnosis is important in order that treatment may be initiated which, in addition to reducing the social and psychological repercussions of incontinence may avert kidney damage with renal scarring and loss of function..

Nevertheless, despite their clinical importance, daytime symptoms suggestive of voiding dysfunction are not always evident and a trained eye is required to detect them. Parents will often fail to describe daytime symptoms, either because they do not know about them or because they consider them normal. Other parents may attribute urge incontinence to laziness on the part of the child who plays until the last moment instead of going straight to the bathroom as soon as an urge is felt or who does not go to the toilet before leaving home and so always needs to stop en route in order to avoid leakage. Usually it is the nocturnal voiding that motivates them to seek medical advice along with all the disturbance it causes: pajamas, bedclothes and mattress all wet; parents' sleep interrupted; the child socially isolated by the embarrassment involved and suffering from low self-esteem; siblings' lives affected; among many others. Thus, technically well-founded, detailed anamnesis is of fundamental importance to the evaluation and classification of these patients.

Urodynamics analysis enables the confirmation of a lower urinary tract dysfunction diagnosis. Analyses can be performed of bladder storage and emptying functions and also of urethra sphincter activity. Pressure can be recorded during filling and emptying of the bladder (cystometry) and urinary flow can be monitored (uroflowmetry) as can external urethral sphincter function (electromyography). For enuretic patients Urodynamics analysis is indicated in the following circumstances: if neurological abnormalities are suspected, when there are diurnal urination abnormalities with no obvious primary pathology, with adolescents presenting nocturnal enuresis resistant to therapy, when there is soiling associated, if voiding difficulties appear after treatment for urinary infection, in cases of recurrent

urinary infection despite the use of chemoprophylaxis, where there is bladder trabeculation or a coiled urethra visible with voiding cystourethrography.<sup>1,9-11</sup>

Urodynamics analysis, however, is not always available. Furthermore it is considered an invasive examination due to the need for urethral catheterization. If it were possible to ascertain whether data obtained from clinical examinations of enuretic patients is capable of indicating the presence of bladder dysfunction a useful contribution would be made towards early diagnosis and treatment.

This study was performed with the following objective:

– Estimate the predictive power of diurnal symptoms for a diagnosis of voiding dysfunction in enuretic children and adolescents treated at the Urodynamics Clinic at the Instituto Fernandes Figueira.

## Methods

This was a cross-sectional study of 91 patients of both sexes aged between 5 and 17 years, suffering either from monosymptomatic nocturnal enuresis or from nocturnal enuresis associated with diurnal voiding dysfunction, referred to the Pediatric Urodynamics Clinic at the Instituto Fernandes Figueira – Fundação Oswaldo Cruz during the period between June 1999 and May 2002. An enuresis frequency equal to or greater than once a week was used as an inclusion criterion for the study.

As this is an cross-sectional study involving dichotomous variables, the rules described by Browner et al. were used to calculate the n value required for an  $\alpha$  error of 0.05 and a  $\beta$  of 0.10. This calculation returned a minimum n value of 23 patients.<sup>14</sup>

The following groups of patients were excluded from the study:

- those suffering from: urological, anorectal or lower limb orthopedic malformations; encephalopathy; obvious neural tube defects; chronic renal failure; diabetes or other clinical conditions which would explain their incontinence;
- those who were on anticholinergics, imipramine, DDAVP or other drugs that act on the detrusor or urethral sphincter at the time of their first consultation.

After approval had been obtained for the project from the Committee for Ethics in Research at the Instituto Fernandes Figueira (CERIFF), specialists and pediatricians working at primary and secondary health centers were informed of its existence in the hope of widening the sample base. This enabled enuretic patients to be referred irrespective of their clinical characteristics (mono/multisymptomatic) and of any clinical suspicion of lower urinary tract dysfunction. As the research progressed children and adolescents began to arrive having been recommended by patients at the Urodynamics Clinic. Once their parents had given their consent the research protocol was applied to these patients too.

The first consultation consisted of anamnesis and a physical examination; laboratory tests and voiding maps were requested.

The voiding maps recorded all nocturnal enuresis episodes for two weeks and all urination and diurnal voiding during the weekend.

All anamnesis was performed by the researcher herself. A model was developed (Figure 1) including objective questions about each diurnal urinary symptom. Also included were: reason for referral, number of enuresis episodes while asleep, per week and per night, bowel function in terms of constipation and/or soiling, history of urinary tract infection, the history of the pregnancy, delivery and neonatal period, neuropsychomotor development history, family history.

The urination frequency that was considered normal was between 4 and 8 times a day.<sup>15-17</sup> This was assessed using the voiding map records and during anamnesis by asking how many times the child had been to the bathroom while waiting for their consultation and/or since they got up. In this way, the possibility that the answer depended entirely on the, often subjective, assessment of the parent or guardian was avoided.

During the physical examination emphasis was given to the search for neurocutaneous stigmata in the lumbar region, to neurological or orthopedic abnormalities and to the examination of external genitalia.

Urodynamics assessment was performed with the children cooperating; with no sedation or containment. Equipment by Dantec was used, either the Duet or Dynamed model, belonging to the Pediatric Urodynamics Laboratory at the Instituto Fernandes Figueira. Bladders were filled with saline solution at 0.9% at room temperature (on average 25 to 30 °C), infused at a rate of 10% of the minimum estimated bladder capacity for age per minute.<sup>6,18</sup>

All results were classified by the same examiner according to International Children's Continence Society.<sup>6</sup>

According to this classification system, Urodynamics findings are considered normal when the bladder can be filled at low pressures and there is increased internal bladder pressure during the voiding phase followed by relaxation of the urethral sphincter complex triggering urination and complete emptying of the bladder. During the fill phase there should be no involuntary contractions or detrusor inhibition.

In order to estimate the probability that the patients' enuresis were due to bladder dysfunction based on diurnal urinary symptoms, positive and negative predictive powers were calculated.

Associations were evaluated between voiding dysfunction as diagnosed by Urodynamics assessment and the following variables: frequency of enuresis episodes, diurnal voiding behavior abnormalities, primary or secondary enuresis onset, family history of enuresis, previous history of urinary infection, bowel dysfunction.

Fisher's exact test was used in order to ascertain whether these associations were statistically significant. This choice was based on the fact that the expected frequency was less than 5, which violates one of the conditions for  $\chi^2$  applicability.<sup>19</sup> The significance level adopted for  $\alpha$  (alpha) was 0.05. Additionally, the relative risk (odds ratio) of a patient presenting voiding dysfunction in conjunction with each of these factors.<sup>20,21</sup>

## Results

One hundred and two patients referred to the IFF Urodynamics Clinic between June 1999 and May 2002 for enuresis were included in the study. Ninety-one of these patients completed the diagnostic protocol. Among those who did not complete the process were three children who refused the urodynamic examination.

Patient age varied from 5 to 17 years. Forty-five (49.5%) patients were female and 46 (50.5%) were male ( $p > 0.882$ ).

Patient distribution according to number of enuresis episodes per week can be observed in Table 1. The fact that 93.4% presented three or more episodes per week stands out.

**Table 1** - Proportional distribution of patients according to the frequency of episodes of nocturnal enuresis

Nights per week	Number of patients	Percentage of patients (%)
6-7	64	70.3
3-5	21	23.1
1-2	6	6.6

The patients had been referred by: pediatricians (63.4%), nephrologists (15.6%), other Urodynamics clinic patients (15.6%) and others (5.5%).

Initial attendance was motivated by nocturnal enuresis in 57 (62.6%) cases and nocturnal enuresis associated with diurnal signs and symptoms in 34 (37.4%). After directed anamnesis and the completion of a voiding map, these patients were reclassified by enuresis type. Anamnesis identified diurnal symptoms in 71 (97.3%) patients allowing for correct diagnosis of enuresis type. In just two (2.7%) patients, elevated urination frequency was observed by means of the voiding map, but not detected by anamnesis.

As can be seen in the graph in Figure 2, after reclassification the number of monosymptomatic nocturnal enuresis sufferers (MNE) fell from 57 (62.6%) to 18 (31.6%) and the number of polysymptomatic sufferers increased from 34 (37.4%) to 73 (68.4%) ( $p < 0.001$ ). Even excluding patients who were referred by laypeople

**Name:** \_\_\_\_\_

**Medical record:** \_\_\_\_\_ **Date of first medical visit:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_

**Sex:** 1 ( ) F 2 ( ) M **Date of birth:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ **Age:** \_\_\_\_\_

**Address:** \_\_\_\_\_

**Phone:** \_\_\_\_\_

**Mother:** \_\_\_\_\_ **Father:** \_\_\_\_\_

**Caregiver:** \_\_\_\_\_

**Referred by:** 1 ( ) pediatrician of other unit 2 ( ) IFF pediatrician 3 ( ) nephrologist 4 ( ) patient of urodynamics  
5 ( ) general practitioner 9 ( ) unknown Others: \_\_\_\_\_

**Reason for referral or main complaint:** 1 ( ) enuresis 2 ( ) enuresis + daily symptoms

**Nocturnal enuresis:**  
Nights per week: 1 ( ) 6-7 2 ( ) 3-5 3 ( ) 1-2  
Episodes of involuntary urine loss per night: 1 ( ) one 2 ( ) >one, 9 ( ) unknown  
Beginning: 1 ( ) primary 2 ( ) secondary

**Daily symptoms:**  
Urinary frequency: \_\_\_\_\_ normal ( ) reduced ( ) increased ( )  
Waiting time in the hospital *versus* number of times of restroom use: \_\_\_\_\_  
Urine stream: ( ) strong ( ) dribbling ( ) interrupted ( ) involuntary flow ( ) dribbling all the time ( ) unknown  
Difficulties to start urinating? Y ( ) N ( ) Urgency? Y ( ) N ( )  
Urgency/enuresis? Y ( ) N ( ) Leakage of urine comes into contact with underwear? Y ( ) N ( )  
Unnoticed urine leakage? Y ( ) N ( ) Excessive dribbling after urinating? Y ( ) N ( )  
Holding technique? Y ( ) N ( )

**Daily symptoms:** 0 ( ) Y 1 ( ) N 9 ( ) unknown

**Measures taken up to this date to achieve sphincter control**  
The child is willing to control? Y ( ) N ( )  
Has the child seen any doctor or other health professional? Y ( ) N ( )  
History of previous treatment: 0 ( ) absent 1 ( ) guidance 2 ( ) propanteline bromide  
3 ( ) oxybutinin 4 ( ) imipramine 5 ( ) desmopressine 6 ( ) alarm 7 ( ) homeopathy  
8 ( ) physical exercises 9 ( ) unknown 10 ( ) others: \_\_\_\_\_

**Intestinal function:** 0 ( ) normal 1 ( ) constipation 2 ( ) fecal leakage 9 ( ) unknown

**History of urinary infection:** 0 ( ) N 1 ( ) Y Number of cases: \_\_\_\_\_

**Pregnancy, delivery and neonatal history:**  
gestational diabetes Y ( ) N ( ) preterm Y ( ) N ( ) respiratory suffering Y ( ) N ( ) cyanosis Y ( ) N ( )  
seizure Y ( ) N ( ) sepsis Y ( ) N ( ) jaundice Y ( ) N ( )  
0 ( ) normal 1 ( ) risk factor for CNS lesion 2 ( ) gestational diabetes 9 ( ) unknown

**Development history:** 0 ( ) normal 1 ( ) delayed 9 ( ) unknown  
Difficulty in the sphincter training with late success Y ( ) N ( )  
Who lives in the same house? father ( ) mother ( ) both ( ) Other: \_\_\_\_\_  
How many siblings does the child have? \_\_\_\_\_

**Stress factors:** 0 ( ) N 1 ( ) Y 9 ( ) unknown  
If the answer for the question above is yes, has your child presented this kind of problem regarding urine control before? N ( ) Y ( )

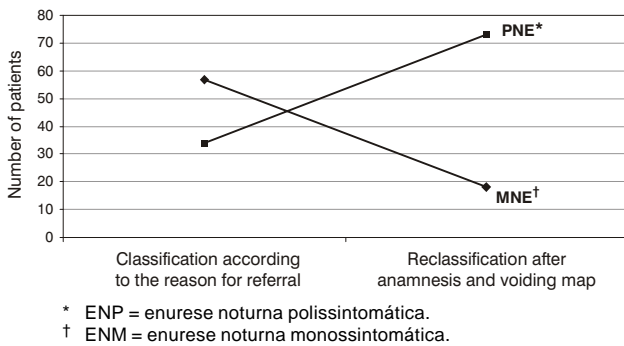
**Family history for enuresis:** 0 ( ) negative 1 ( ) positive 9 ( ) unknown  
father ( ) mother ( ) brothers ( ) sisters ( ) father's family ( ) mother's family

**Nocturia (parents):** 0 ( ) N 1 ( ) Y 9 ( ) unknown Who: \_\_\_\_\_

**Figure 1** - Model of anamnesis used with enuretic patients in order to perform the diagnostic investigation of bladder dysfunction

(Urodynamics patients and a teacher) and taking into account only those patients who had been referred by a doctor, the difference between pre and post reclassification remained statistically significant.

Excluding these patients the number of MNE sufferers dropped from 46 (60.5%) to 15 (19.7%) and the number of polysymptomatic enuresis sufferers increased from 30 (39.5%) to 61 (80.3%) ( $p < 0.001$ ).



**Figure 2** - Classification regarding the type of enuresis (monosymptomatic or polysymptomatic) according to the referral and reclassification of these patients after anamnesis and voiding map

Urodynamics findings were compatible with voiding dysfunction in 86 (94.5%) cases. Fourteen (77.8%) of these were suffering from MNE and 72 (98.6%) of them presented diurnal symptoms in association with nocturnal enuresis (Table 2). The main Urodynamics abnormalities found were: reduced bladder capacity in 76 (83.5%) patients and uninhibited contractions in 62 (68.1%). Four (4.4%) patients presented post-voiding contraction.

**Table 2** - Results of urodynamics according to the presence or absence of associated daily symptoms

	Total	Normal urodynamics	Abnormal urodynamics
<b>MNE*</b>	18 (100%)	4 (22.2%)	14 (77.8%)
<b>PNE †</b>	73 (100%)	1 (1.4%)	72 (98.6%)
<b>Total</b>	91 (100%)	5 (5.5%)	86 (94.5%)

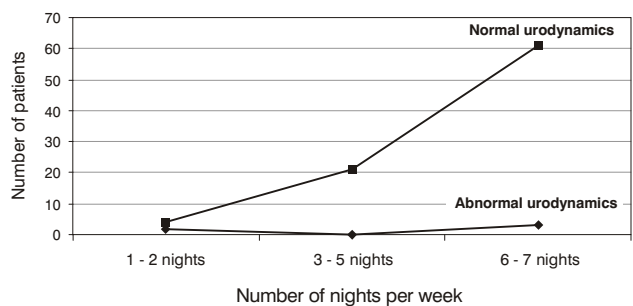
\* Monosymptomatic nocturnal enuresis  
 † Polysymptomatic nocturnal enuresis.

Voiding dysfunction was more common among patients with higher numbers of nocturnal enuresis episodes per week ( $p = 0.005$ ). Patients suffering from two or less episodes of nocturnal enuresis per week had a lower risk of presenting voiding dysfunction than those who experienced three or more episodes per week (odds ratio = 0.07; 95% confidence interval:  $0.01 < OR < 0.87$ ;  $p = 0.033$ ) (Figure 3).

There was an association between presence/absence of diurnal symptoms, as detected by anamnesis and notes on the map, and voiding dysfunction as verified by the Fisher test ( $p < 0.005$ ). The risk of Urodynamics findings being abnormal was around 20 times greater among patients who presented diurnal symptoms (odds ratio =

20.27; 95% confidence interval:  $1.87 < OR < 532.00$ ) than for patients suffering from MNE.

The use of anamnesis together with the voiding map to detect diurnal urination pattern abnormalities returned a high positive predictive value for a diagnosis of voiding dysfunction. Thus, the probability that any given patient with diurnal symptoms associated with nocturnal enuresis would present voiding dysfunction was 98.6%. In contrast, however, the probability that a patient with MNE would not present voiding dysfunction (negative predictive value) was just 22.2%. The proportion of patients with voiding dysfunction who presented diurnal symptoms associated with nocturnal enuresis (sensitivity) was 83.7%. The proportion of patients with without voiding dysfunction who presented MNE (specificity) was 80%.



**Figure 3** - Proportional distribution of bladder dysfunction according to the number of nights with enuresis per week

The presence of diurnal urination symptoms was the primary risk factor for a diagnosis of voiding dysfunction among the children e adolescents. There was also a statistical association between voiding dysfunction and the following factors: case history suggestive of CNS damage and an enuresis frequency greater than three nights per week. All of these are detectable by anamnesis – an instrument that is inherent to medical consultations. The results of analysis of the remaining variables such as: primary or secondary onset, bowel dysfunction, previous history of urinary infection, a perinatal history at risk of CNS damage and family enuresis history can be seen in Table 3.

**Discussion**

Our study revealed an elevated percentage of voiding dysfunction sufferers among children treated for enuresis at the Urodynamics Clinic of the Instituto Fernandes Figueira. This percentage was greater than those found in other studies.<sup>22,23</sup>

**Table 3** - Analysis of the risk factors for bladder dysfunction

Characteristics	Odds ratio	Confidence interval	p
Primary or secondary beginning	0.65	0.06 < OR < 16.87	p = 0.546
Bowel dysfunction	3.46	0.43 < OR < 32.25	p = 0.183
Urinary infection	-	-	p = 0.324
Perinatal history	-	-	p < 0.001
Family history	0	0 < OR < 2.51	p = 0.328

The frequency of nocturnal wetting exhibited a statistically significant association with voiding dysfunction. Patients suffering more than three enuresis episodes per week also presented a higher risk of voiding dysfunction. The high percentage of patients wetting more than three nights a week may have contributed to the high dysfunction prevalence found.

The fact that the Instituto Fernandes Figueira is a center of excellence in the field of pediatric urodynamics may also cause a selection bias towards patients with a clinical suspicion of voiding dysfunction. Making the research project public through basic health centers and deciding to accept patients referred by other patients were methods for reducing this bias. These two sources were responsible for the inclusion, of more than half of the study population.

The majority of the patients (62.7%) were referred by pediatricians, which was largely an expression of the response to publicizing the research project. This provides evidence of the importance of making pediatricians aware of the possibility of clinical recognition of voiding dysfunction among patients suffering from enuresis, since they are who care for these children in the first instance.

Patients referred for MNE represented 62.6% of those included in the study. However, after anamnesis and the voiding map were applied, only 19.8% of the patients remained in this category. If the group of patients referred by doctors are considered in isolation, the reduction in MNE sufferers after anamnesis was also significant. Literature reviews reinforce the impression that, after more detailed analysis, the percentage of patients with MNE tends to drop. Chandra claims that 48% of boys and 70% of girls referred to their service due to nocturnal enuresis only, also presented diurnal symptoms.<sup>3</sup> Similarly, an earlier study in which we compared the reason for the referral of 72 children suffering from enuresis or urinary incontinence with a diagnosis after directed anamnesis,

showed that more than half of the children referred for nocturnal enuresis also presented diurnal symptoms not previously noted.<sup>24</sup> These findings appear, at least partly, to be related to the conception of enuresis as exclusively a behavioral problem or as a family inheritance that will improve over time. Added to this is the average pediatrician's unfamiliarity with voiding functions and the difficulty of clinical identification of diurnal urinary dysfunctional symptoms. The MNE proportions found after reclassification (19.8%) were lower than those described in other studies. Rawashdeh et al.<sup>25</sup> found 74.1%, Yang et al.<sup>26</sup> 48%, Cigna et al.<sup>23</sup> 25.7% of MNE. The lack of agreement is probably due to methodological differences, such as the details of the anamnesis model, and the bias referred to earlier.

Work which lists more rigorous methodological criteria for diurnal symptoms in general involves smaller samples, using less than 20 patients.<sup>27,28</sup> Glazener & Evans performed a systematic analysis of the use of alarms with children with nocturnal enuresis. Of the 952 potentially relevant primary studies, only 22 were of sufficient quality to be included in the analysis and of these only four excluded patients with diurnal symptoms.<sup>29</sup>

Some of the most important publications on nocturnal enuresis prevalence, such as the classic by Fergusson et al., were written more than twenty years ago. At that time, current voiding dysfunction knowledge did not exist and the emphasis on separating MNE from enuresis associated with other urinary, intestinal or neurological symptoms.<sup>30</sup>

These facts provide evidence of the need for systematic research into diurnal symptoms by means of directed anamnesis and voiding map. The validity of the anamnesis model employed has been demonstrated by its ability to identify the existence of voiding abnormalities in 97.3% of those affected. The importance of this screening process becomes evident when we consider that the risk of an enuretic patient having voiding dysfunction is 20 times

greater when diurnal symptoms are exhibited in association. Both anamnesis and the voiding map are diagnosis instruments available to any doctor, at no cost and with high predictive values for voiding dysfunction diagnosis .

This being the case, due to its high positive predictive value, anamnesis in conjunction with the voiding map as a tool for identifying diurnal symptoms, has been shown to be an important instrument for voiding dysfunction diagnosis. The lower negative predictive value draws our attention to the possibility, although less common, is also possible with MNE.

The study results reveal a discrepancy between current knowledge about voiding dysfunction and its application in clinical practice, which makes clear the need to publicize this information.

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