

Research Article

# Adult Neurogenic Lower Urinary Tract Dysfunction in Amyotrophic Lateral Sclerosis

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## Abstract

**Aims:** To determine the presence of adult neurogenic lower urinary tract dysfunction (ANLUTD) symptoms in Amyotrophic Lateral Sclerosis (ALS), to identify the underlying urodynamic findings and to treat and to prevent urinary complications in this already devastating disease.

**Materials and Methods:** We present 8 clinical cases that we found fortuitously on consulting Neuromuscular Dystrophies at the Physical Medicine and Rehabilitation (PMR) Department. We applied an ANLUTD Questionnaire by the authors according to the International Continence Society (ICS). All patients underwent urodynamic studies. We reviewed the published literature on ANLUTD in ALS in the Pubmed database up to September 2019.

**Results:** Our sample comprised 7 female patients and 1 male, all with ANLUTD. The filling symptoms were urge urinary incontinence (UUI) in 4 patients and reduced bladder sensation in 2 patients. The emptying symptoms were abdominal straining with urinary retention in 1 patient, urinary retention in 1 other patient, hesitancy in 1 patient and slow stream in another. Only two out of eight patients had both filling and emptying symptoms (reduced bladder sensation and urinary retention).

All cases underwent urodynamic study (UDS), five of them with changes, namely 2 reduced bladder sensation, 2 detrusor over activity (DO), 1 detrusor sphincter dyssynergia (DSD) with high residual volume (350ml) and 1 acontractile detrusor also with high residual volume (420ml).

We found clinical urodynamic correlation in only 4 patients, including the two cases with high residual volume.

In the literature, we found only 3 articles about ANLUTD assessment in ALS and, curiously, with high prevalence: 41% in a sample of 54 patients, 33% in 43 patients and 44% in 55 patients. Only one study performed a UDS, which showed changes in 9 out of 10 patients.

**Conclusion:** The literature is still scant but the prevalence of filling and emptying symptoms is high in ALS.

We found that most symptomatic patients had urodynamic changes. We observed clinical urodynamic correlation in only half of the patients, including two cases with high residual volume.

Given the ANLUTD urodynamic observations, we, like other authors, think that ALS seems to achieve also brainstem reticular formation and intermediolateral nucleus in the spinal cord grey matter.

All patients with ALS should therefore be questioned about ANLUTD and the post void residual volume should be evaluated. UDS should be performed because it optimises therapeutic orientation and allows the risk of high urinary tract complications to be avoided. Given the relevance of the topic, further high-quality studies are needed for early recognition and to take measures that improve patients' quality of life.

**Keywords:** Amyotrophic lateral sclerosis; ANLUTD; Amyotrophic lateral sclerosis and ANLUTD; Amyotrophic lateral sclerosis and urodynamic study

## Introduction

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that primarily affects motor neurons in the motor cortex,

brainstem and spinal cord with features of first-order and second-order neurons [1]. First-order neuron signs occur by corticospinal and corticobulbar tracts lesion and those of the second-order neuron by brainstem nucleus lesion and anterior horn lesion in the medulla

[1].

The literature considers adult neurogenic lower urinary tract dysfunction (ANLUTD) as atypical in ALS or resulting from the lower mobility of these patients, with disease progression [2,3]. In fact, there seems to be a selectivity in the neurons that are affected and in those that are not. The Oculomotor, Trochlear and Onuf nuclei are usually spared [4-7].

Fortuitously, we found 8 cases with symptoms referred by the caregiver or by the patient on consulting Neuromuscular Dystrophies at the Physical Medicine and Rehabilitation (PMR) Department of Centro Hospitalar Universitário do Porto (CHUP); So we did a bibliographical research on the subject and found a prevalence of 33% to 44% in the literature [8-10].

The aims of this study were to determine the presence of ANLUTD in ALS, to identify the underlying urodynamic findings, to study the clinical urodynamic correlation in order to question ANLUTD in the future, and to treat and to prevent complications in this already devastating disease.

## Materials and Methods

We present 8 cases of Neuromuscular Dystrophies consulted in the PMR Department of CHUP with symptoms of urinary tract dysfunction referred by the patients themselves or their caregivers. We apply the *ANLUTD Questionnaire* by the authors, according to the *International Continence Society* (ICS) standards [11]. None of our patients had diabetes mellitus or alcohol habits.

All patients performed a urodynamic study (UDS) under the ICS recommendations of good urodynamic practice and the international ICS report on the terminology for ANLUTD [11,12]. A dipstick test was routinely performed before each UDS in order to exclude any concomitant urinary tract infection. UDS were done using the MMS Database<sup>®</sup> system with perineal surface electromyography (EMG).

A review of the published literature on ANLUTD and UDS in ALS in the *Pubmed* database was carried out until September 2019 using the keywords: “amyotrophic lateral sclerosis”, “ANLUTD”, “amyotrophic lateral sclerosis and ANLUTD” and “amyotrophic lateral sclerosis and urodynamic study”.

## Results

Our sample comprised 8 cases, 7 females and 1 male, with a mean age of 59 years and an average disease evolution of 2.6 years at the time of the urinary complaints (Table 1). All of them had ANLUTD. Four patients presented only with storage symptoms (UUI), 2 had only void symptoms (1 hesitancy and 1 slow stream) and 2 had mixed symptoms (1 patient with reduced bladder sensation, straining to void and urinary retention, and another also with reduced bladder sensation and urinary retention).

The 8 patients performed a UDS, which was normal in 3 cases and changed in 5 cases (Table 2). We found clinical-urodynamic correlation in 4 out of 8 (Table 2). One of them presented a reduced sensation to urinate, needed straining to void (Credé manoeuvre) and her UDS corroborated the reduced bladder sensation and voiding with detrusor contraction concurrent with an involuntary urethral sphincter contraction, which is called detrusor-sphincter dyssynergia

**Table 1:** Demographic and clinical characteristics of our sample.

Case	Genre	Age (y)	Disease evolution (y)
A	Female	39	1.5
B	Male	28	1
C	Female	63	2
D	Female	71	1
E	Female	76	3
F	Female	56	5
G	Female	78	4
H	Female	59	3

**Key:** Y-Years.

(DSD). This patient had a too high residual volume (RV) – 350mL. She also had a renovesical ultrasound with hydronephrosis and pyelocaliceal ectasia. The second one presented also with reduced bladder sensation and urinary retention. The urodynamic data revealed decreased bladder sensation and acontractile detrusor. She was unable to urinate with manoeuvre and VR was 420ml. The third case presented UUI with detrusor overactivity (DO) during storage, underactivity detrusor during the mictional stage but only 13ml RV. The fourth case had UUI with DO.

In the 4 patients without clinical-urodynamic correlation, 2 had UUI with a normal urodynamic study, 1 had emptying symptoms, also with a normal urodynamic study, and the last had emptying symptoms and DO.

Regarding the bibliography, we find only 3 publications on ANLUTD in ALS (Table 3). Arlandis et al, in the 2017 study, in a sample of 55 patients with ALS, found 24 (44%) with ANLUTD, 83% of whom had mixed symptoms; only ten agree to do a UDS and the most frequent findings were detrusor overactivity combined with non-relaxing external sphincter during voiding.12 There is no reference to altered sensitivity in urodynamics.

Nubling et al, in 2014, in a sample of 43 patients, found 14 (32%) ANLUTD patients, of whom 73% were UUI.10.

Lopes de Carvalho et al, in 2011, in a sample of 54 patients (41%), found 22 patients with symptoms [9].

## Discussion

ANLUTD is considered atypical in ALS or results from reduced mobility. The 8 cases that we came across led us to carry out a more detailed study of ANLUTD in ALS.

When analyzing results, the literature shows a high prevalence of ANLUTD in ALS, 33% to 44% in samples of 50 patients [8-10]. The most frequently documented symptoms are mixed (83%) 8 and UUI alone (26-73%) [8,10].

In our sample of 8 patients, 4 presented only with storage symptoms (UUI), 2 had only void symptoms (1 hesitancy and 1 slow stream) and 2 had mixed symptoms (1 patient with reduced bladder sensation, straining to void and urinary retention, and another also with reduced bladder sensation and urinary retention).

Regarding the UDS, we found only one study in the literature that performed UDS in ALS. This showed changes in 9 out of 10 patients.

**Table 2:** Clinical and urodynamic characterization of our sample.

CASE	ANLUTD	ANLUTD (ICS)	UDS	Clinical-urodynamic correlation
A	UUI	Filling	Normal filling and emptying	Without correlation
B	UUI	Filling	Normal filling and emptying	Without correlation
C	UUI	Filling	Increased bladder sensation; normal bladder compliance; able to urinate with detrusor pressures of 13cm H <sub>2</sub> O; normal flow; RV 12mL	With correlation
D	UUI	Filling	DO; Decreased compliance; Underactivity detrusor with pressure of 9cm H <sub>2</sub> O at 300mL; VR 13mL	With correlation
E	Hesitancy	Emptying	Normal filling and emptying	Without correlation
F	Slow Stream	Emptying	Normal sensation; DO; able to urinate with detrusor pressures of 34cm H <sub>2</sub> O; RV 26mL	Without correlation
G	Decreased desire to urinate Abdominal straining Urinary retention ITUs	Filling Emptying	Reduced bladder sensation; normal bladder compliance; voiding with DSD; RV 350mL	With correlation
H	Decreased desire to urinate Urinary retention	Filling Emptying	Reduced bladder sensation; high bladder compliance; acontractile detrusor; no sphincter relaxation while attempting urination; unable to urinate voluntarily or with manoeuvres; RV 420ml	With correlation

**Key:** ANLUTD: Adult Neurogenic Lower Urinary Tract Dysfunction; DO: Detrusor Overactivity; DSD: Detrusor-Sphincter Dyssynergia; UDS: Urodynamic Study; ICS: International Continence Society; UUI: Urgency Urinary Incontinence; RV: Residual Volume.

**Table 3:** Results found in the literature.

Authors	N	ANLUTD	UDS	Urodynamic changes	Clinical-urodynamic correlation
Arlandis, 2017	55	24/55 (44%) 83% mixed symptoms; 26% UUI alone	10/24 (42%)	1/10 UDS N 9/10 UDS changed: 9/9 DSD (100%) 7/9 Do (78%) 3/9 RV > 150mL (33%)	Not studied
Nubling, 2014	43	14/43 (33%) 73% UUI	-	-	-
Lopes Carvalho, 2011	54	22/54 (41%) Symptoms unspecified	-	-	-

**Key:** ANLUTD: Adult Neurogenic Lower Urinary Tract Dysfunction; DSD: Detrusor-Sphincter Dyssynergia; N: Number of Samples; DO: Detrusor Overactivity; UDS: Urodynamic Study; UUI: Urgency Urinary Incontinence; RV: Residual Volume.

The most frequent findings were DO and non-relaxing external sphincter [8].

In our study, the 5 changed UDS revealed 2 with reduced bladder sensation, 2 with DO, 1 with DSD and high RV (350ml) and 1 with acontractile detrusor and also high RV (420ml).

Regarding the clinical-urodynamic correlation, this has not been studied in the literature. In our sample, we had clinical-urodynamic correlation in only 4 patients, including the two cases with high RV.

There is increasing evidence that ALS is a multisystemic disease [2,8,13]. In addition to affecting pyramidal and corticobulbar tracts, brainstem nucleus and anterior horn in the medulla, some authors report the achievement of brainstem reticular formation and the intermediolateral nucleus in the grey region of the spinal cord [2,3,8].

The periaqueductal grey (PAG) matter in the brainstem's reticular formation receives projections from many higher brain centres and also controls the primary input to the pontine micturition centre (PMC) [14,15]. DO could thus be justified by the lack of encephalic inhibition on the PMC and non-relaxing urethral sphincter or DSD due to lack of excitation on the PMC. Normally, the PMC would activate the descending pathways causing urethral relaxation and bladder contraction. Lesion at the PMC or supra sacral spinal cord may lead to DO and DSD [11].

The PAG also receives and passes sensitive bladder signals to higher brain centres [14,15]. If compromised, this sensitivity information will be changed. We had two patients with reduced bladder sensation, one of them with normal bladder compliance; so, this change could be due not to a bladder distension but rather to a

possible compromise at reticular formation level.

We found one patient with urodynamic alterations compatible with acontractile detrusor; as a matter of fact, some studies revealed the involvement of the medullary grey region at the level of the parasympathetic-sacred grey region [2,3,8].

Regarding the Onuf nucleus, located in the ventral horn of the sacral spinal cord, damage of this structure affects sphincters and some of the pelvic musculature and thus stress incontinence may result [11]; we did not find urodynamic data suggestive of its attainment. In fact, there seems to be a selectivity in the neurones that are affected and in those that are not [4-7]. Elevated levels of glutamate - an important neurotransmitter in signal processing, which at high levels is excitotoxic leading to axonal degeneration, are documented in ALS [16-22]. It is reported in the literature that the oculomotor, trochlear and Onuf receptors have been found to act as sensors for glutamate homeostasis, performing a protective function [1,4-7].

Considering the high percentage of ANLUTD (33-44% in literature), the high residual volumes, the urodynamic changes found and the lack of clinical-urodynamic correlation, it therefore seems fundamental to question the patients, evaluate the residual volumes and perform a USD to optimise the therapeutic management in order to avoid the risk of high urinary system complications in this already devastating disease.

## Conclusions

ANLUTD in ALS is poorly known and therefore not questioned in consultation. Literature is still scarce but the prevalence of filling and emptying symptoms is high in ALS.

In our study with all the patients with ANLUTD, we observed a slight predominance of storage symptoms. However, we found that voiding dysfunction can be severe with raised residual volume and high urinary tract dysfunction.

Most of the ANLUTD patients in this ALS study had urodynamic changes.

We observed clinical-urodynamic correlation in only half of our patients, including in patients with severe voiding dysfunction.

Given the ANLUTD urodynamic changes that we observed, namely reduced bladder sensation, DO, DSD and acontractile detrusor, we, like others authors, think that ALS seems also to achieve brainstem reticular formation and intermediolateral nucleus in the spinal cord grey region.

All patients with ALS should therefore be questioned about ANLUTD and the post void residual volume should be evaluated. UDS must be performed because it optimises therapeutic orientation and allows the risk of high urinary tract complications to be avoided. Given the topic relevance, further high-quality studies are needed for early recognition and to take measures that improve patients' quality of life.

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