

Prioritization of risk situations in neuro-urology: guidelines from Association Française d'Urologie (AFU), Association Francophone Internationale des Groupes d'Animation de la Paraplégie (A.F.I.G.A.P.), Groupe de Neuro-urologie de Langue Française (GENULF), Société Française de Médecine Physique et de Réadaptation (SOFMER) and Société Interdisciplinaire Francophone d'UroDynamique et de Pelvi-Périnéologie (SIFUD-PP).

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A steering committee included urologists and physical medicine and rehabilitation practitioners. Based on a literature review and their own expertise, they established a comprehensive risk-situation list and built a risk scale, allowing multiple other experts to score each clinical situation. New recommendations were generated using a Delphi process approach.

Forty-nine experts participated in the rating group. Among the 206 initial items, 163 were selected and divided into four domains, diagnosis and assessment, treatment, follow-up, and complications, and two sub-domains, general (applicable for all neurological conditions) and condition-specific [varying according to the neurological condition (spinal cord injury, multiple sclerosis, brain injury, Parkinsonism, dysraphism, lower motor neuron lesions)]. The resulted guidelines are expert opinions established by a panel of French-speaking specialists, which could limit the scalability of this work.

The present multidisciplinary collaborative work generates recommendations which complement existing guidelines and help clinicians to reorganize their patients' list in the long term with a personalized medicine approach, in the context of health crisis or not.

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Management of patients with neurogenic lower urinary tract dysfunction (NLUTD) is well established; aiming to prevent complications and to improve patients' quality of life [1]. Before the COVID-19 pandemic, the guidelines of scientific societies focused on the initial assessment, the therapeutic management, and the long-term follow-up, mainly in spinal cord injured (SCI), multiple sclerosis (MS), and patients with dysraphism [2 – 4]. However, no specific timeline for each step of the management and no prioritization of risk situations have been included in the current existing guidelines.

The current health crisis has drastically impacted patient management in many fields, including neuro-urology, leading to a mandatory reorganization. To improve practices and to help setting priorities, scientific societies established recommendations in an emergency context to postpone a large majority of patients' assessment and non-urgent treatments [5 – 7]. Since the virus continues to spread, recommendations helping to reorganize the diagnosis, treatment, and follow-up of neuro-urological patients are required to prevent urological complications and to preserve patients' quality of life. The present work aimed to establish guidelines regarding the prioritization and optimal timing of each step of NLUTD management.

A steering committee with recognized expertise in neuro-urology was created, including urologists and physical medicine and rehabilitation (PMR) practitioners (Supplementary material 1). The ten members were involved in French-speaking scientific societies: AFU (French Association of Urology), SOFMER (French Society of Physical and Rehabilitation Medicine), SIFUD-PP (French-speaking Interdisciplinary Society of Urodynamics and Pelvi-Perineology), and GENULF (French-speaking Neuro-Urology Working Group). The role of the steering committee was to devise the comprehensive risk-situation list, build the risk scale for participants, score each clinical situation, and generate recommendations using a Delphi process.

All risk factors for complications inherent to NLUTD, ranging from purely functional to life-threatening complications, were listed based on a systematic literature review conducted by the steering committee. The research was conducted in May 2020 using the Medline and Embase databases, without date limitation. All articles written in French or English were eligible. Only studies that considered the following outcomes were included: upper urinary-tract complications, hydronephrosis, chronic kidney disease, urinary-tract infections, urolithiasis, device erosion, device infection, death, anxiety/depression, social impairment, quality of life impairment. The complete research algorithm is described in Supplementary material 2. Additional searches were included after the selection of the key articles.

Out of the 2036 articles selected (1937 articles from the literature review and 99 additional ones), 192 had a level of evidence $\geq 2b$ according to the Oxford classification [8]. The steering committee drafted a list of 206 proposals depicting the various risk situations identified from their expertise and the literature review. Four domains were described: diagnosis , treatment , follow-up , and complications, and split between the members of the steering committee (Supplementary material 1). Two sub-domains were also established: general (applicable for all neurological conditions) and condition-specific [varying according to the neurological condition (spinal cord injury, multiple sclerosis, brain injury, Parkinsonism, dysraphism and lower motor neuron lesions)].

To define each situation's level of risk, we used the Global Risk Analyzing[9 , 10]. Five levels of risk were defined, and the timing of healthcare for each level of risk was validated by a group of 16 experts using a Delphi process: no delay, less than 1 month, 1–6 months, 6–12 months, over 12 months (supplementary material 3).

The 206 propositions were divided into 5 groups with a balanced number of items, and split between the experts according to their field of competence.

A panel of French-speaking specialists from different disciplines (urology, PMR, gynecology, and pediatric urology), with extensive neuro-urology experience, was selected and split into 5 groups to rank the proposals submitted by the steering group. All the experts were members of at least one of the following French-speaking scientific societies: AFIGAP (International French-speaking Association of Paraplegia), AFU, SOFMER, SIFUD-PP, and GENULF.

Experts were asked to grade the level of risk according to the aforementioned risk scale for clinical scenarios in the first rating round. If an inter-rater's agreement of $\geq 90\%$ was reached, the proposition and the level of risk were accepted. Otherwise, the proposition with the predominantly designated level of risk was selected after validation by the steering committee and submitted to further rounds. From the second round, each expert rated individual propositions on a scale ranging from 1 (totally inappropriate proposal) to 7 (totally appropriate proposal). Agreement level was defined according to the French health authority recommendations to build Delphi-based guidelines [11]. The proposals for which an agreement was not reached during the two first rounds were submitted to a third round, and a fourth round if necessary, giving the median score for each as a feedback to the panel. The definitions of agreement are depicted in supplementary material 4.

Forty-nine experts participated in the rating group. The experts were divided into different rating subgroups according to their subspecialty (Supplementary table 5).

Among the 206 initial proposals, 163 were accepted after the final rating process (Supplementary material 4).

The initial assessment is an essential step of lower urinary tract symptoms management since it contributes to the diagnosis of an underlying neurological condition. No studies have been done to determine the timeframe in which patients with NLUTD should be assessed, and the potential harm resulting from an increase in this assessment time. Twenty-one general items and 4 SCI patient-specific items were validated after the Delphi process. The guidelines on initial assessment are reported in Table 1 and supplementary material 6 and 7. Table 1 Diagnosis—general population

Bold: strong agreement; **non-bold:** relative agreement. The full table is available in supplementary material 6

NLUTD neurogenic lower urinary tract dysfunction

The neuro-urological treatment often combines the management of the bladder reservoir and of the voiding mechanism. Despite randomized controlled studies and well-established treatment algorithms [1], there is not sufficient data in the literature to recommend the timing to initiate treatment of detrusor overactivity with a high level of evidence. For the voiding mechanism, evidence demonstrated that indwelling urethral catheters increased the risk of urological complications (urinary tract infections, lithiasis, bladder cancer, devastated bladder outlet) in patients with NLUTD. Urethral intermittent self-catheterization remains the best voiding modality for most patients with chronic urinary retention and should be introduced as soon as possible [12]. The scoring validated 18 general items and 39 condition-specific items. The guidelines on treatments are reported in Table 2 and supplementary material 8. Table 2 Treatment—general population

Bold: strong agreement; **non-bold:** relative agreement

NLUTD neurogenic lower urinary tract dysfunction

Follow-up is one of the cornerstones of NLUTD management. Some previous guidelines recommended an annual follow-up of SCI patients, patients with MS and dysraphism [2 – 4]. They are based on the “bladder risk factor” of urinary tract deterioration. The definition of a “high risk” bladder remains controversial. However, a cut-off of 40 cmH₂O discriminating high vs low detrusor pressure and 20 ml/cmH₂O dichotomizing lower or normal bladder compliance are mainly used [13 , 14].

Despite this, no robust data is available to assess the optimal follow-up schedule in patients with NLUTD. The scoring validated 19 general items and 18 condition-specific items. The guidelines on follow-up are reported in Table 3 and supplementary material 9 and 10. Table 3 Follow-up—general population

Bold: strong agreement; **non-bold:** relative agreement. The full table is available in supplementary material 9

NLUTD neurogenic lower urinary tract dysfunction

NLUTD complications are numerous, including urinary tract infections, lithiasis, reflux and renal failure. In addition, specific complications should be addressed, such as sores, cognitive and functional impairment, and autonomic dysreflexia. There is no robust data available regarding the optimal timing to manage previous complications. The Delphi scoring validated 42 general items and 2 items specific to SCI patients. The guidelines on complications are reported in Table 4 and supplementary material 11 and 12. Table 4 Complications—general population

Bold: strong agreement; **non-bold:** relative agreement. The full table is available in supplementary material 11

NLUTD neurogenic lower urinary tract dysfunction

To the best of our knowledge, the present work provides the first grading risk-situation guidelines in patients with NLUTD. In the existing guidelines established when the COVID-19 pandemic started, patients with NLUTD were barely considered, and often lumped together with functional urology, which was not considered as an emergency condition by a few scientific societies [7 , 15 – 17]. Only the EAU [18 , 19], the AFU [5], and the ICS[20] described the neurologic population and suggested a management schedule for these patients in times of health crisis. Our present guidelines are in accordance with many aspects to existing guidelines. However, several specific factors have been addressed, allowing a significant improvement in current recommendations.

Considering the initial assessment and the diagnosis, these new guidelines are consistent with existing recommendations, which suggest an early assessment in both congenital and acquired neurological diseases to diagnose NLUTD to prevent irreversible deterioration of the lower and upper urinary tract [21]. The optimal timeline was defined in SCI patients, with an assessment as soon as possible after the end of the spinal shock phase and urodynamic testing at 6 and 12 months after the initial injury. The GENULF suggested performing a urodynamic testing every six months [2] within the two first years. Based on the specificities of the neurological patients and their risk factors, we proposed individual guidelines and a schedule for assessment and treatment relative to each individual situation. For example, we recommended a neuro-urological assessment as a matter of emergency in the case of autonomic dysreflexia without any obvious etiology and a reassessment of the treatment efficacy in the following month in the case of identified neuro-urological cause.

The assessment following treatment would depend on the therapy. The delay to introduce a treatment has not been characterized in the literature until the COVID-19 pandemic, which has led to new recommendations to face this crisis. The scientific societies proposed to postpone patients' management with different delays depending on the severity of the pathology [5 , 18 – 20]. In addition to these recommendations built for short time crisis, we propose a risk-level based timeframe for NLUTD management, applicable in a context of sanitary crisis or not. For example, a surgical alternative in case of refractory detrusor overactivity should be proposed within a month in SCI patients with high risk, but within 1 to 6 months in MS patients.

The follow-up has been well standardized. The ICS recommended annual urological monitoring, to detect complications and to adjust bladder management [22]. More specifically, Schurch et al. and the GENULF recommended in patients with dysraphism or spinal cord injury a yearly examination because of their “high-risk” bladder, which could be delayed by one to two years after attaining controlled NLUTD [2 , 3]. De Sèze et al. recommended a cystometry every one to three years in MS patients [4]. In more general terms, the EAU recommended in “high-risk” patients, to assess upper urinary tract every 6 months and perform a physical and urine laboratory examination every year [21]. However, during the crisis, most of the scientific societies proposed postponing urodynamic assessment [5 , 20]. Only Goldman et al. proposed to assess neurogenic patients with urodynamic with up to 4 weeks of delay [23]. We recommend an assessment every 6–12 months in patients with initially “high risk” NLUTD, based on the urodynamics, regardless of the pathology. In patients with “low risk”, this assessment should be done after 12 months.

Concerning emergency procedures, as previously recommended by all scientific societies, they should not be delayed. However, we also underscored SCI patients' specific complications which required urgent treatment such as Brindley device impairment or autonomic dysreflexia resulting from urolithiasis.

However, we must acknowledge several limitations to the present study. Indeed, the literature review has not been able to bring out enough data to drive recommendations with a high level of evidence. These guidelines are, therefore, an expert opinion. Moreover, these recommendations were established by a panel of French specialists, and some situations may not respond to another system of care, limiting the scalability of this work. Care organisation and resources should differ between countries, leading to difficulties to apply strictly these recommendations. However, due to the robust methodology and the exhaustiveness of the work, they shall help most clinicians to manage their patients.

This multidisciplinary collaborative work helped to establish recommendations which may be complementary with existing guidelines. By creating a comprehensive risk scale listing all relevant clinical situations encountered in neuro-urology, these recommendations would help clinicians to reorganize their patients' list in the long term with a personalized medicine approach, whatever is the situation.

Below is the link to the electronic supplementary material. Supplementary file1 (PDF 553 KB)

French Society of Physical and Rehabilitation Medicine

French-speaking Interdisciplinary Society of Urodynamics and Pelvi-Perineology

French-speaking Neuro-Urology Working Group

International French-speaking Association of Paraplegia

Neurogenic lower urinary tract dysfunction

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