

# Surveillance Strategies for Neurogenic Lower Urinary Tract Dysfunction



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## KEYWORDS

- Neurogenic bladder • Neurogenic lower urinary tract dysfunction (NLUTD) • Surveillance
- Spinal cord injury • Urodynamics

## KEY POINTS

- Individuals with neurogenic lower urinary tract dysfunction (NLUTD) are at high risk for complications, including upper tract/renal deterioration and bladder cancer.
- Surveillance for individuals with NLUTD using diagnostic tests, such as urine analysis, renal laboratory tests, imaging, urodynamics, and cystoscopy, may help prevent serious complications.
- Guidelines for NLUTD from multiple organizations review the evidence for available surveillance strategies and make wide-ranging recommendations.
- Guideline recommendations for surveillance in NLUTD are supported by limited evidence suggesting the need for development and testing of standardized protocols.

## INTRODUCTION

According to the International Continence Society, the definition of neurogenic lower urinary tract dysfunction (NLUTD) is: “lower urinary tract dysfunction due to disturbance of the neurologic control mechanisms. Neurogenic lower urinary tract dysfunction thus can be diagnosed in presence of neurological pathology only.”<sup>1</sup> The broad nature of this definition, which includes bladder or urethral dysfunction resulting from insults to the brain, spinal cord, ganglia, or peripheral nerves is, in part, what makes the establishment of evidence-based surveillance strategies so challenging. Add to this the fact that the causes of neurologic injury can be equally wide ranging and include medical conditions, neurologic disease, trauma, cancer, infection, inflammation,

and ischemia, and the complexity inherent in the term NLUTD becomes quite daunting. Perhaps we are in an era of understanding of NLUTD that is like the time, in the middle of the 20th century when “Cancer” was considered a mysterious, single entity, and not a myriad of conditions that we now know to be defined by very specific genetic mutations. As an eerie reflection of our own limited understanding of NLUTD, we may remember that the overwhelming majority of clinicians in the early 1960s reported that they would not tell their patients about the diagnosis of a cancer for fear of irreparable psychological harm.<sup>2</sup>

## WHY PERFORM SURVEILLANCE?

NLUTD is associated with a wide range of complications,<sup>3,4</sup> including recurrent UTIs, stones, fistulae,

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incontinence, skin breakdown, traumatic hypospadias, urethral erosion, and autonomic dysreflexia. However, the 2 complications that have been most widely studied and that lead to significant morbidity and mortality have been upper tract deterioration and increased risk of bladder malignancy. Most of the data about these complications in individuals with NLUTD is obtained from the population with spinal cord injury and disorders (SCI&D).

### ***Bladder Cancer***

Bladder cancer is a main cause of increased morbidity and mortality in individuals with NLUTD. Major risk factors for bladder cancer include smoking, chronic urinary tract infections (UTI) and/or inflammation, bladder calculi, and exposure to toxins.<sup>5</sup> Indwelling catheters cause chronic inflammation, which, in turn, may lead to an increased risk of bladder cancer.<sup>6</sup>

Welk and colleagues<sup>7</sup> performed a literature review looking at the incidence of bladder cancer, age at the time of bladder cancer diagnosis, disease invasiveness, and cancer-specific mortality in 21 separate studies of individuals with SCI&D. The investigators concluded that the incidence of bladder cancer in SCI&D was 16 times higher than in individuals without SCI&D (0.32% vs 0.02%), equivalent to 32 patients per 100,000 in SCI&D and 2 per 100,000 in the general population. Likewise, they found that the mean age of bladder cancer was more than a decade earlier in SCI&D (48–61 years of age) compared with non-SCI (60–70 years of age). Across the studies reviewed, the investigators identified that 58% to 100% of individuals with SCI&D presented with muscle invasive disease at the time of diagnosis, compared with only 25% of the general population.<sup>7</sup> Importantly, the gold standard for treatment of muscle-invasive bladder cancer is a radical cystectomy and urinary diversion using an intestinal segment, a treatment associated with high complication rates in this population.<sup>8</sup> In addition, the overall 5-year survival rate for all patients with muscle invasive bladder cancer is only 50%.<sup>9</sup> Finally, cancer-specific mortality was found to be much higher in SCI&D, ranging from 12% to 57%. This cancer-specific mortality rate was 71% greater compared with individuals without SCI&D.<sup>7</sup>

In a large study of US Veterans, West and colleagues<sup>10</sup> reviewed data from 33,500 Veterans with SCI&D and identified 130 with a diagnosis of bladder cancer. These investigators found that the 1-year survival was 61% and the 5-year survival was only 31%. This poor survival data speaks to the very lethal nature of bladder cancer

in this specific population. Unfortunately, the type of bladder management was only available in 42 of these 130 Veterans (32%), limiting understanding of potential risk factors.<sup>10</sup>

Risk factors for bladder cancer in SCI&D have been investigated and include indwelling Foley catheters, chronic UTIs, smoking, bladder calculi, increased urine contact, and immune dysregulation. In the Veterans Affairs study discussed above,<sup>10</sup> 62% of SCI&D individuals with bladder cancer used indwelling Foley or suprapubic catheters and 38% used other means for bladder management. This suggests that indwelling catheters increase the risk for patients with NLUTD, but that indwelling catheter use is not the ONLY significant risk factor.

### ***Upper Tract Deterioration***

The other major urologic complication of NLUTD leading to increased morbidity and mortality is upper tract deterioration. Upper tract changes can manifest as new onset hydronephrosis or acute kidney injury (AKI). Although the exact pathophysiology of how NLUT directly leads to upper tract deterioration and AKI has not been elucidated, 2 urodynamic risk factors have been identified. These risk factors include poor detrusor compliance and increased intravesical pressures.

Detrusor compliance is defined as the change in detrusor volume divided by the change in detrusor pressure ( $\Delta V/\Delta P$ ) during the urodynamic filling phase.<sup>11</sup> Reduced (poor) compliance can occur when there are structural changes in the detrusor, mediated by replacement of the detrusor smooth muscle with collagen and fibrosis.<sup>12,13</sup> This increase in stiffness is associated with reduced capacity, vesicoureteral reflux, and elevated intravesical pressures. Poor compliance often occurs with longstanding obstruction as in NLUTD in which there is obstruction due to detrusor sphincter dyssynergia.

Although exact values for poor compliance have not been explicitly defined, several researchers have examined the question. Hackler and colleagues<sup>14</sup> examined compliance measurements in SCI&D and found that 69% with compliance values less than 20 mL/cmH<sub>2</sub>O had signs of upper tract deterioration on renal imaging (mainly hydronephrosis) as compared with only 21% with compliance values greater than 20. Based on this, they proposed that a cutoff value for poor compliance should be 20 mL/cmH<sub>2</sub>O. Weld and colleagues<sup>15</sup> found that the highest rates of renal damage were seen with compliance values less than 12.5 mL/cmH<sub>2</sub>O. The lack of specificity of these cutoff values for poor compliance is one of

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