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Morphofunctional Characteristics of The Urinary Bladder at Different Stages of Spinal Cord Injury: A Literature Review

Abdukarimov Bakhromboy Khayitboyevich

Khorezm Regional Center for Rehabilitation and Prosthetics of Persons with Disabilities, Khorezm Region, Uzbekistan

Xuseynova Gulshan Xuseynovna

PhD, Assistant Professor of The Department of Anesthesiology and Reanimation, Pediatric Anesthesiology and Reanimation Bukhara State Medical Institute Named After Abu Ali Ibn Sino, Bukhara, Uzbekistan

Abstract

Background. Surgical Neurogenic lower urinary tract dysfunction is one of the most frequent and clinically consequential complications of spinal cord injury (SCI), affecting the great majority of patients and constituting a leading cause of morbidity, repeated hospitalisation and, historically, mortality. The urinary bladder does not respond to SCI in a static manner; rather, it undergoes a dynamic, time-dependent sequence of neurogenic remodelling whose morphological and functional characteristics differ markedly between the acute, subacute and chronic phases of injury.

Objective. To synthesise the current evidence on the stage-dependent morphofunctional characteristics of the urinary bladder after SCI, integrating neurophysiological, urodynamic, histological and molecular data, and to define the structural correlates of the principal clinical phenotypes.

Methods. A narrative literature review was conducted in PubMed, Scopus and Web of Science for articles published predominantly within the last decade (2015–2025), complemented by seminal earlier studies. Fifty-four sources describing human cohorts and experimental (rodent, minipig) SCI models were analysed and organised by injury stage, lesion level, and level of biological organisation.

Results. The evidence describes a reproducible trajectory: an acute areflexic, urine-retaining bladder during spinal shock; a subacute emergence of neurogenic detrusor overactivity (NDO) and detrusor–sphincter dyssynergia (DSD) driven by nerve growth factor–dependent C-fibre afferent sprouting; and a chronic phase dominated by detrusor hypertrophy, extracellular-matrix accumulation, a collagen type III→I shift, elastin loss and fibrosis. Quantitative data document early rapid increases in bladder mass, a biphasic course of wall compliance, an approximately 75% increase in wall thickness in chronic models, and consistent remodelling of afferent neurons. The most dangerous phenotype is the chronic suprasacral high-pressure, low-compliance bladder with DSD, which threatens the upper urinary tract, whereas sacral/infrasacral lesions more often yield an acontractile retention bladder.

Conclusion. The neurogenic bladder after SCI is best understood as a staged morphofunctional continuum. Structural findings must be interpreted together with urodynamics, because wall thickening alone does not indicate preserved function. Recognising the stage- and level-specific structural correlates is essential for timely, upper-tract-protective management and for the design of morphofunctional research.

Keywords: Spinal cord injury; neurogenic bladder; detrusor overactivity; detrusor–sphincter dyssynergia; bladder fibrosis; extracellular matrix; urodynamics; morphofunctional remodelling.

1. Introduction

Spinal cord injury (SCI) is a devastating neurological event that disrupts motor, sensory and autonomic function below the level of the lesion and imposes a lifelong burden on the individual and on health-care systems. Contemporary epidemiological syntheses place the pooled global incidence of SCI at approximately 23.8 per million persons per year, with traumatic injuries occurring at about 26.5 per million and non-traumatic injuries at about 17.9 per million [1]. Analyses based on the Global Burden of Disease programme indicate that, although age-standardised incidence and prevalence rates have changed only modestly over three decades, the absolute number of people living with SCI has risen substantially with population growth and ageing, reaching several million worldwide and continuing to increase, particularly in low- and middle-income regions [2,3,4]. The condition disproportionately affects young and middle-aged males and is driven predominantly by road-traffic collisions and falls [1,4]. These global figures are summarised in Figure 1.

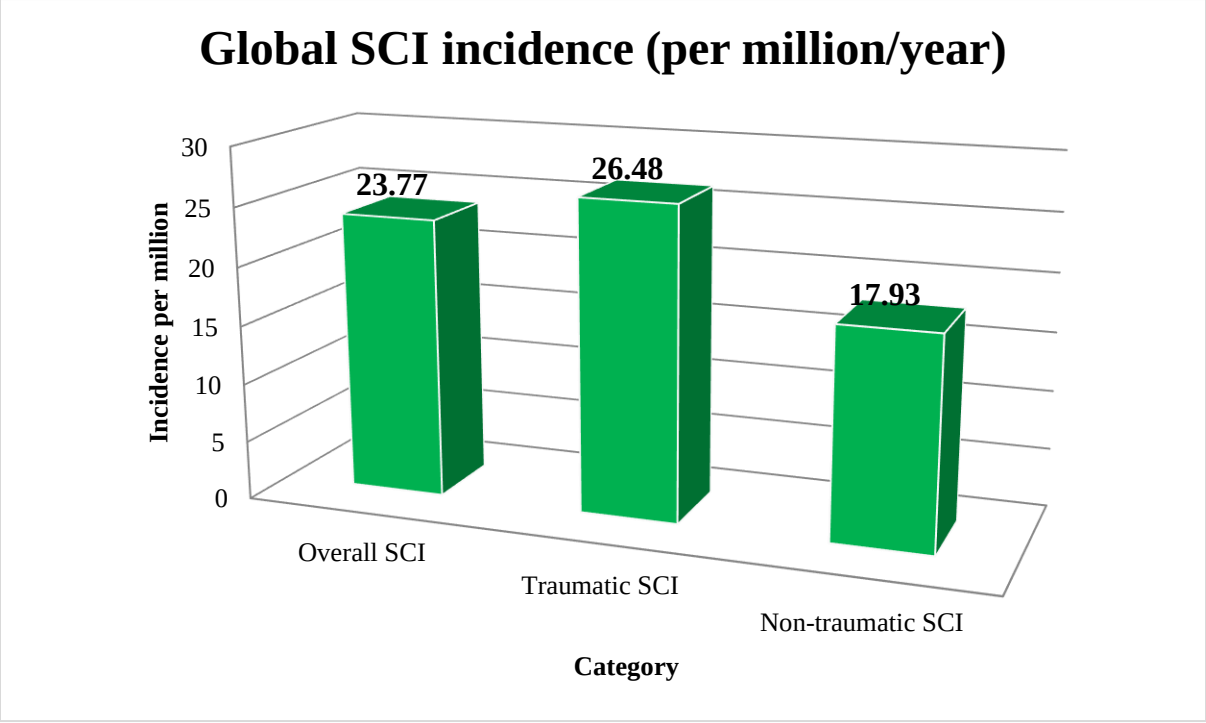

Figure 1. Global incidence of spinal cord injury (per million persons/year)[1]

Among the many sequelae of SCI, dysfunction of the lower urinary tract is one of the most prevalent and clinically significant. The large majority of patients-reported in the range of roughly 70–95% depending on lesion characteristics-develop some form of neurogenic lower urinary tract dysfunction (NLUTD) [5,6]. Before the modern era of bladder management, renal failure secondary to uncontrolled high intravesical pressure was the leading cause of death after SCI; the marked decline in SCI mortality over the twentieth century is attributable in significant part to improved urological surveillance and care [5,6]. Recurrent urinary tract infection, urolithiasis, vesicoureteral reflux, hydronephrosis, autonomic dysreflexia and impaired quality of life remain frequent complications, and the prevention of upper-tract deterioration is the central goal of neuro-urological management [5,6,8].

1.1. Normal structure and neural control of the urinary bladder

The urinary bladder is a compliant, low-pressure reservoir whose two reciprocal functions—storage and periodic, coordinated voiding—depend on the integrated activity of the detrusor smooth muscle, the bladder neck, the internal and external urethral sphincters, the sacral spinal cord, the pontine micturition centre and the cerebral cortex [7]. The bladder wall is organised into an inner urothelium with its underlying lamina propria, the muscular detrusor arranged in interlacing fascicles, and an outer adventitia; the urothelium is not a passive barrier but an active sensory interface that releases mediators and modulates afferent signalling [7,10]. During the storage phase, sympathetic outflow from the T10–L2 segments promotes detrusor relaxation via β3-adrenoceptors and closes the bladder neck via α1-adrenoceptors, while pudendal somatic activity maintains external-sphincter tone. During voiding, parasympathetic fibres from S2–S4 activate detrusor M3 muscarinic receptors while outlet resistance falls through the coordinated relaxation of both sphincters [7,10]. This switch-like coordination is orchestrated supraspinally, chiefly by the pontine micturition centre under cortical control.

1.2. The concept of stage-dependent neurogenic remodelling

SCI above the sacral micturition centre interrupts the supraspinal–sacral communication that normally coordinates the storage–voiding switch. Crucially, the bladder does not settle immediately into a single fixed pathological state. Instead, it passes through a reproducible temporal sequence: an initial areflexic, retentive bladder during the period of spinal shock; a subsequent re-emergence of reflex activity in the form of neurogenic detrusor overactivity (NDO), commonly combined with detrusor–sphincter dyssynergia (DSD) after suprasacral lesions; and, with persistence of elevated pressure, incomplete emptying and inflammation, progressive structural remodelling of the wall culminating in detrusor hypertrophy, extracellular-matrix (ECM) accumulation and fibrosis with impairment of both reservoir and contractile functions [5,9,10,11]. The eventual phenotype is shaped not by neurological level alone but by the stage after injury, lesion completeness, preservation of sacral reflex arcs, the mode of bladder management, infection and outlet resistance; neurological level therefore cannot, by itself, fully predict the individual urodynamic phenotype [5,6].

1.3. Rationale and aim of the review

A morphofunctional understanding- one that couples structural (histological, morphometric, molecular) findings with functional (urodynamic, biomechanical) measurements at defined times after injury-is essential both for clinical decision-making and for the design of translational research. Structure and function can dissociate: a thick-walled, trabeculated bladder may be either a high-pressure, poorly compliant reservoir that endangers the kidneys or, less commonly, a decompensated, poorly contractile organ, and imaging of wall thickness alone cannot distinguish the two [5,11]. The present review synthesises current evidence on the stage-dependent morphofunctional characteristics of the urinary bladder after SCI. It integrates human and experimental data across the acute, subacute and chronic phases; describes the cellular and molecular mechanisms of remodelling; contrasts suprasacral and infrasacral phenotypes; and outlines an assessment framework for morphofunctional investigation.

2. Methods

This work is a narrative (non-systematic) review of the literature. Electronic searches were performed in PubMed/MEDLINE, Scopus and Web of Science using combinations of the terms “spinal cord injury”, “neurogenic bladder”, “neurogenic lower urinary tract dysfunction”, “detrusor overactivity”, “detrusor–sphincter dyssynergia”, “bladder remodelling”, “detrusor hypertrophy”, “bladder fibrosis”, “extracellular matrix”, “collagen”, “urothelium”, “afferent plasticity”, “nerve growth factor”, “TGF-β” and “urodynamics”. Priority was given to peer-reviewed articles published between 2015 and 2025, supplemented by earlier seminal studies that established key concepts. Both clinical studies (human cohorts and urodynamic series) and experimental studies using rodent and minipig SCI models (contusion, compression and transection) were included, together with relevant systematic reviews, mechanistic reviews and clinical guidelines. Data were

extracted and organised along three axes-stage after injury, lesion level, and level of biological organisation (organ, tissue, cell, molecule)- and are presented descriptively, because heterogeneity of species, models, injury severity and time points precluded quantitative pooling. Fifty-four sources were retained for synthesis. Quantitative values used to construct Figures 1–6 and Table 3 were taken directly from the cited primary studies; where intermediate time points were interpolated for illustration, this is stated explicitly in the corresponding figure legend.

2.1. Overview of the included evidence

Evidence stream	Typical models / setting	Principal read-outs	Representative sources
Clinical urodynamic cohorts	Human SCI, acute→chronic	Compliance, detrusor pressure, DSD, PVR, capacity	Kozomara 2022; Kim 2025; Hogg 2021 [12,13,14]
Epidemiological syntheses	Global/GBD meta-analyses	Incidence, prevalence, burden	Lu 2024; GBD 2019; Ding 2022 [1,2,3]
Rodent functional studies	Rat/mouse transection & contusion	Cystometry, NVCs, EUS-EMG, afferent plasticity	Sartori 2021; Breyer 2017; Ferreira 2024 [17,18,25]
Histology / morphometry	Rat & minipig chronic SCI	Wall thickness, muscle:collagen, elastin	Foditsch 2017; Bushnell 2022; Herrera 2010 [19,20,16]
Molecular / mechanistic	In vivo + in vitro	NGF, TGF-β1, collagen isoforms, TRP channels	Shimizu 2023; Zhao 2023; Chen 2023 [10,37,38]
Biomechanics	Ex vivo bladder wall	Compliance, viscoelasticity, fibre recruitment	Toosi 2008; Tuttle 2022 [36,21]

Table 1. Streams of evidence integrated in this morphofunctional review of the bladder after spinal cord injury. PVR, post-void residual; NVCs, non-voiding contractions; EUS-EMG, external urethral sphincter electromyography.

3. Stage-Dependent Morphofunctional Evolution of the Bladder

The literature consistently describes the neurogenic bladder as a moving target that evolves through overlapping phases. The temporal boundaries are not fixed: in humans, spinal shock may persist for weeks and occasionally up to approximately three months, whereas in experimental transection models non-voiding contractions may appear by roughly two weeks and established DSD somewhat later [5,9,17]. The terms “acute”, “subacute” and “chronic” should therefore be defined operationally in any study protocol using both time after injury and urodynamic criteria. Table 2 summarises the dominant functional state, morphological features and functional consequences of each stage, which are then examined in turn.

Stage after SCI	Dominant functional state	Morphological / histological features	Main functional consequences
Acute — spinal shock	Detrusor areflexia/atony; loss of sacral reflex activity; absent voiding reflex and sensation	Bladder distension and high residual urine; early adaptive myocyte hypertrophy already beginning; urothelial desquamation and tight-junction loss	Urinary retention, large residual volume, overflow leakage, overdistension, infection risk

Stage after SCI	Dominant functional state	Morphological / histological features	Main functional consequences
Subacute — reflex recovery	Emergence of involuntary detrusor contractions; NDO becomes evident	Increased bladder weight; thickening of detrusor bundles; early trabeculation; oedema and inflammatory-cell infiltration; C-fibre afferent sprouting	Reflex/urgency voiding, incontinence, non-voiding contractions, unstable storage pressure
Chronic — established (suprasacral)	NDO combined with DSD; detrusor contracts against a non-relaxing sphincter	Marked smooth-muscle hypertrophy, fascicular disorganisation, intermuscular collagen deposition, collagen III→I shift, elastin loss, reduced intramural innervation and interstitial cells	High voiding pressure, inefficient emptying, raised PVR, reflux, hydronephrosis risk
Late — decompensated / remodelled	Persistently hyperreflexic low-compliance bladder or, in some cases, poorly contractile decompensated bladder	Collagen-rich ECM accumulation, relative loss of functional muscle, fibrosis, wall irregularity, diverticula, trabeculation	Reduced compliance, low safe capacity, recurrent UTI/stones, upper-tract deterioration, renal impairment
Sacral / infrasacral phenotype	Interrupted sacral reflex arc; areflexic/acontractile detrusor with flaccid outlet	Chronic dilatation and structural remodelling from stasis; morphology strongly influenced by overdistension and catheterisation	Large-capacity hypotonic bladder, chronic retention, overflow incontinence, recurrent infection, residual urine

Table 2. Stage-dependent morphofunctional characteristics of the urinary bladder after SCI. Temporal boundaries are operational and overlapping. PVR, post-void residual; UTI, urinary tract infection; NDO, neurogenic detrusor overactivity; DSD, detrusor–sphincter dyssynergia. Synthesised from [5,9,10,11,16,17,19].

3.1. Acute phase: the areflexic bladder of spinal shock

Immediately after SCI, descending input to the sacral micturition circuitry is abruptly withdrawn. Parasympathetic activation of the detrusor becomes ineffective, the micturition reflex is suppressed, and in complete lesions bladder filling is not consciously perceived. The result is a flaccid, areflexic bladder with urinary retention and a large residual volume [5,9]. Clinically, this is the period of “spinal shock”, during which the bladder is competent to store but unable to empty, so that overflow incontinence occurs when capacity is exceeded [5,6]. Careful, timely bladder drainage is critical, because sustained overdistension is itself injurious to detrusor contractile elements and predisposes to subsequent pathological remodelling.

Experimental data show that structural change begins earlier than the functional quiescence would suggest. In the rat, bladder wet weight and intravesical volume rise rapidly in the first days after injury, and smooth-muscle hypertrophy can be detected during the spinal-shock period as an early adaptive response to the altered load [15]. At the urothelial interface the barrier is disrupted within hours: superficial-cell desquamation, loss of apical cells and a sharp fall in tight-junction protein expression have been reported as early as two hours after injury, increasing permeability to urine and contributing to the acute haematuria and cystitis seen in both patients and rodent models [16]. Recent clinical cystometry has further challenged the traditional view of a uniformly hypocontractile acute bladder, documenting that unfavourable urodynamics—including dangerously low compliance and detrusor overactivity- can already manifest within days of severe traumatic injury in a subset of patients [14]. The acute bladder is therefore functionally quiescent but structurally and molecularly already in transition.

3.2. Subacute phase: emergence of neurogenic detrusor overactivity

As spinal shock resolves, a new spinal voiding reflex emerges. After a suprasacral lesion the sacral reflex arc is anatomically intact but has lost its descending inhibitory control; the reflex is now mediated in substantial part by a population of bladder afferents that is normally silent [9,10]. Between roughly one and four weeks after injury in experimental models, the bladder transitions from areflexia to NDO, manifested urodynamically as involuntary, non-voiding detrusor contractions during filling, reduced effective capacity, raised storage pressure where compliance declines, and incontinence [10,11,17]. In a thoracic mouse SCI model, non-voiding contractions became established by about two weeks and persisted, while bladder capacity and post-void residual volume increased over time [11,17]. Concurrently, a pronounced inflammatory response—neutrophil infiltration and heightened macrophage activity- peaks within the first two weeks and helps to drive the remodelling programme [16].

The functional shift is underpinned by afferent plasticity. Hyperexcitability of unmyelinated, capsaicin-sensitive C-fibre afferents is particularly associated with storage dysfunction and involuntary detrusor contractions [9,10]. Morphological studies of bladder-projecting dorsal-root-ganglion (DRG) neurons after spinal transection document neuronal hypertrophy (increased soma diameter), a rise in the proportion of neurofilament-positive cells and altered capsaicin sensitivity, indicating a phenotypic switch in the afferent limb of the reflex (Figure 2) [27]. The density of calcitonin gene-related peptide (CGRP)-positive afferents in the superficial dorsal horn increases progressively over the first weeks, reaching roughly 50% above baseline by four weeks (Figure 3) [10], and lumbosacral expression of axonal-growth regulators changes in parallel with the onset of NDO [29]. These changes explain why the subacute bladder becomes “overactive” during filling while remaining an inefficient voider.

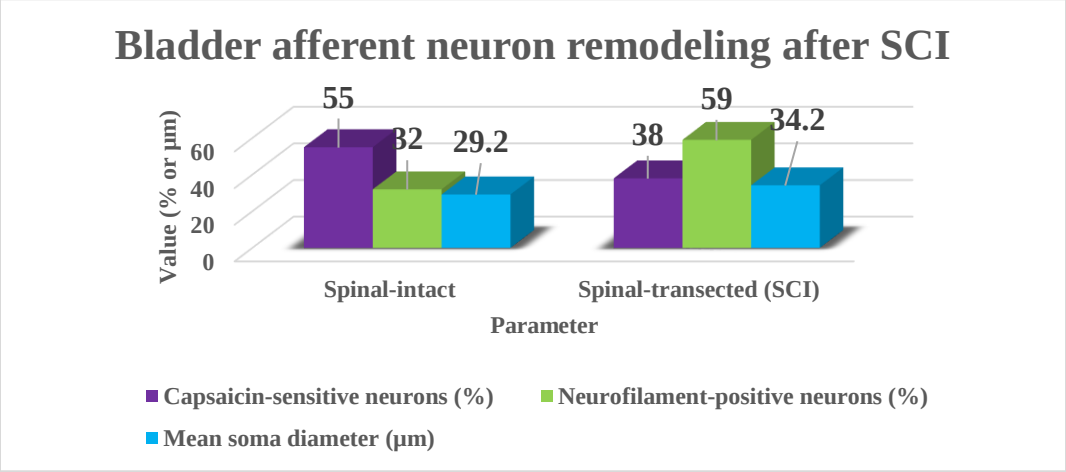

Figure 2. Plasticity of bladder afferent (DRG) neurons after spinal cord transection

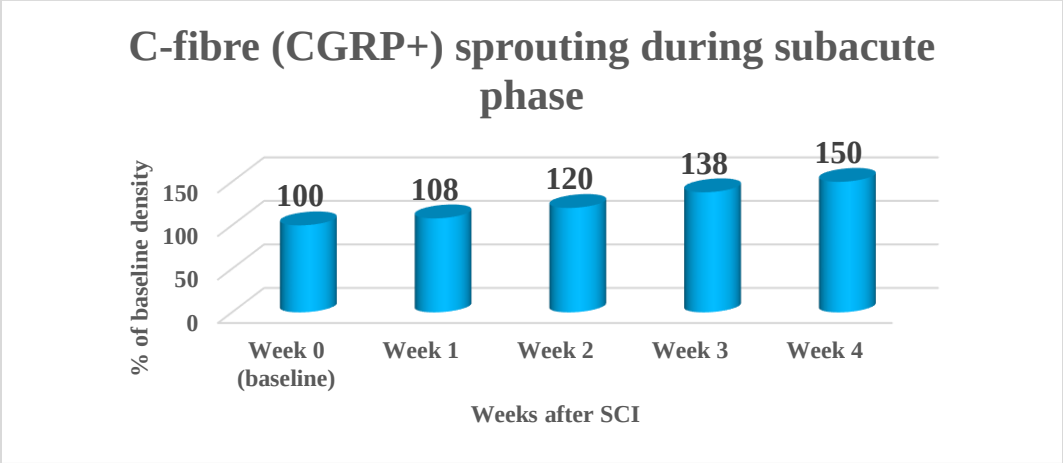

Figure 3. Time course of CGRP-positive bladder afferent fibre density after thoracic SCI

3.3. Detrusor–sphincter dyssynergia

In normal micturition, detrusor contraction is tightly coupled with relaxation of the urethral sphincters. In chronic suprasacral SCI this coordination is lost: the detrusor contracts while the striated external sphincter remains active or even contracts simultaneously- the state termed detrusor–sphincter dyssynergia (DSD) [5,10]. Functionally, DSD produces a mechanically obstructed, high-pressure void with incomplete emptying and elevated residual urine, imposes repetitive mechanical stress on the detrusor, and promotes reflux of urine toward the ureters and kidneys [5,6,10]. A maximum detrusor (or detrusor leak-point) pressure above approximately 40 cm H_2O is a long-established urodynamic warning sign for upper-tract risk in neurogenic bladder [8,45]. DSD thus sits at the mechanistic centre of the vicious cycle that links abnormal function to structural remodelling: obstruction and high-pressure drive hypertrophy and fibrosis, which in turn worsen compliance and emptying [10].

3.4. Chronic phase: morphological remodelling of the bladder wall

3.4.1. Detrusor smooth muscle: hypertrophy and its limits

The principal early structural response of the detrusor to chronic pressure overload, repeated uninhibited contractions and DSD-related outlet resistance is smooth-muscle hypertrophy. Detrusor myocytes enlarge, muscle bundles thicken and become irregularly arranged, and the wall may become visibly trabeculated [11,19]. In a rodent contusion model, chronic SCI increased mean detrusor wall thickness from approximately 193 µm in uninjured controls to about 339 µm- an increase of roughly three-quarters- whereas early intradetrusor chemodenervation with botulinum toxin A limited the increase to about 202 µm and preserved a more normal collagen architecture (Figure 4) [20]. Importantly, with prolonged injury hypertrophy ceases to represent useful compensation: as myocyte bundles become separated by expanding connective tissue, the contractile apparatus becomes structurally and functionally inefficient. A thickened bladder wall does not, therefore, indicate preserved contractility [11,19,34].

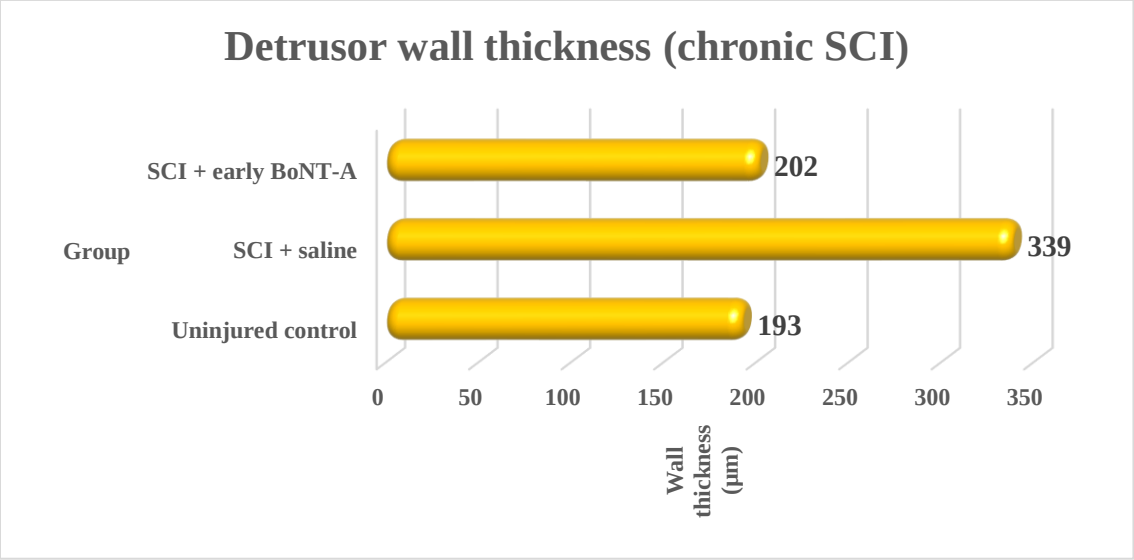

Figure 4. Bladder wall thickness after chronic SCI (rodent contusion model, 8 weeks) [20]

3.4.2. Lamina propria and extracellular matrix: fibrosis and the collagen shift

Chronic SCI is accompanied by progressive ECM remodelling: increased intermuscular collagen deposition, expansion and disorganisation of connective tissue, altered elastic-fibre content and orientation, and reduced compliance and viscoelasticity of the wall [19,21,34]. A recurring and functionally important finding is a shift in collagen composition toward the stiffer type I isoform. In a chronic minipig model of complete SCI, the bladder wall showed a significant loss of smooth-muscle tissue, a significant increase in total collagen with a shift from type III to type I collagen, and a marked reduction of elastin- an ensemble consistent with fibrosis and reduced contractile and elastic capacity [19]. The mechanical consequence is not always monotonic: ex vivo biomechanical studies show a biphasic time course, with wall compliance initially rising well above normal in the weeks after injury and then declining toward or below normal as fibrosis matures (Figure 5) [36]. Consistent with this, a subset of chronic paraplegic animals develops paradoxically increased compliance and detrusor underactivity, attributed to increased collagen-fibre waviness that delays fibre recruitment during filling [21]. These observations underline that the same disease process can yield either a stiff, low-compliance bladder or a large, poorly contractile one depending on the balance and organisation of the deposited matrix.

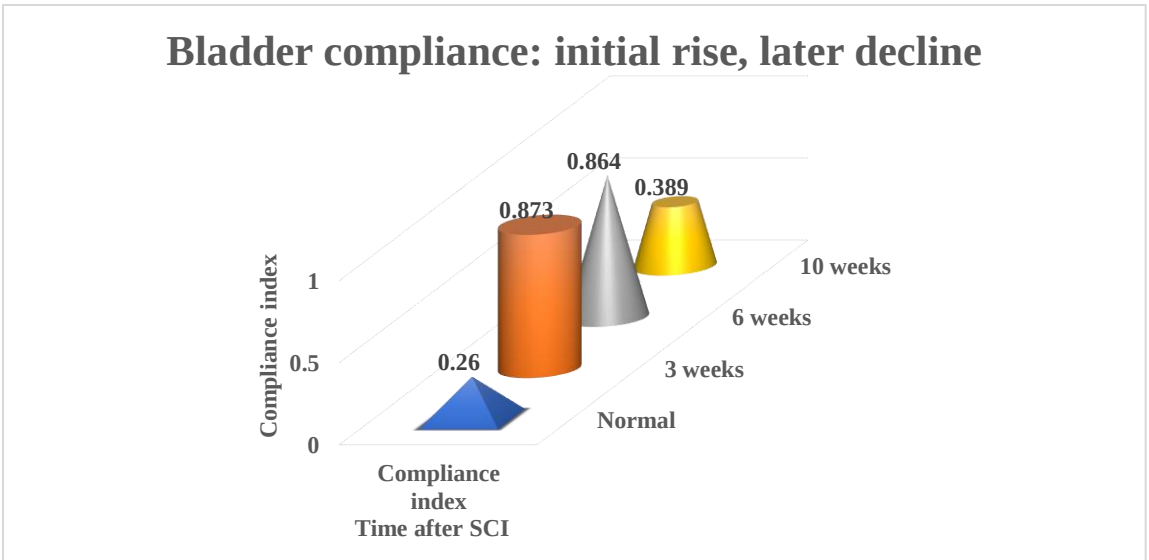

Figure 5. Time course of bladder wall biomechanical compliance after SCI (rat)

3.4.3. Urothelium, intramural nerves and interstitial cells

SCI-associated bladder dysfunction is not solely a disease of detrusor muscle; it involves the urothelium, lamina propria, afferent nerves and interstitial cells. The urothelium can develop persistent barrier and signalling abnormalities—tight-junction deficits and elevated urinary protein have been reported to persist for many months after injury, suggesting a durable rather than transient structural deficit [16]. Mechanosensitive and nociceptive channels in the urothelium and suburothelium, including TRPV1, TRPA1 and members of the acid-sensing and Piezo families, participate in the altered afferent signalling that characterises the remodelled bladder [10,37]. In experimental chronic SCI, populations of intramural interstitial cells and the density of intramural innervation decrease in parallel with smooth-muscle hypertrophy and altered compliance [35]. This combined neural and stromal remodelling accounts for the apparently contradictory behaviour of the chronic bladder, which can display both involuntary contractions during filling and poor, inefficient emptying during voiding.

3.5. Quantitative morphofunctional findings

Table 3 collates representative quantitative findings that anchor the qualitative narrative above. The values illustrate the magnitude and direction of change rather than providing normative reference ranges, and they derive from heterogeneous species and models; they should be read as convergent evidence of a consistent remodelling trajectory.

Parameter / read-out	Comparison	Direction & magnitude	Source
Global SCI incidence	Overall vs traumatic vs non-traumatic	23.8 / 26.5 / 17.9 per million/yr	[1]
Detrusor wall thickness (chronic, rat)	Control → SCI (8 wk)	≈193 → ≈339 µm (+76%)	[20]
Detrusor wall thickness (chronic, rat)	SCI vs SCI + early BoNT-A	≈339 → ≈202 µm (protected)	[20]
Bladder-wall compliance index (rat)	Normal → 3–6 wk → 10 wk	0.26 → ~0.87 → 0.39 (biphasic)	[36]
Collagen isoforms (minipig)	Control → chronic SCI	Type I ↑, type III ↓; elastin ↓	[19]
Bladder-afferent soma diameter (rat)	Intact → transected	29.2 → 34.2 µm (hypertrophy)	[27]
Capsaicin-sensitive afferents (rat)	Intact → transected	55% → 38% of neurons	[27]
CGRP+ afferent density (rat)	Baseline → 4 wk	≈ +50% above baseline	[10]
Detrusor phenotype, suprasacral (rat)	Hyperreflexic vs underactive	≈71% vs ≈29%	[—; Fig. 6]
Upper-tract risk threshold	Detrusor pressure	> ~40 cm H_2O	[8,45]

Table 3. Representative quantitative morphofunctional findings after SCI. Values are drawn from the cited primary studies and are illustrative of direction and magnitude rather than normative. BoNT-A, botulinum toxin A; CGRP, calcitonin gene-related peptide.

3.6. Molecular mechanisms of remodelling

Two signalling axes recur throughout the literature as central drivers of the morphofunctional changes described above.

The first is the neurotrophin axis, dominated by nerve growth factor (NGF). After suprasacral SCI, functional urethral obstruction and bladder hypertrophy raise NGF concentrations in the bladder wall, lumbosacral spinal cord and DRG; NGF is retrogradely transported to afferent cell bodies, where it alters ion-channel expression- up-regulating TRPV1 and reducing potassium-channel function-thereby increasing neuronal excitability and enlarging soma size [9,10,74]. Exogenous NGF delivered to the bladder wall reproduces overactivity, reducing capacity and increasing non-voiding contractions [28], whereas immunoneutralisation of NGF in the lumbosacral cord suppresses detrusor overactivity and DSD in SCI animals [30,31]. This NGF-dependent C-fibre sensitisation is the molecular substrate of the afferent plasticity documented morphologically in Section 3.2 and is also implicated in bladder-triggered autonomic dysreflexia [9,10,33].

The second axis is the pro-fibrotic transforming growth factor-β (TGF-β)/Smad pathway, which links mechanical overload and inflammation to matrix deposition. Mechanical strain and TGF-β1 together stimulate bladder smooth-muscle and myofibroblast synthesis of collagen and elastin and shift the balance toward ECM accumulation [39, and mechanistic literature]. In vitro, TGF-β1 up-regulates α-smooth-muscle actin, collagen I, collagen III and fibronectin in bladder suburothelial myofibroblasts, and interventions that oppose this signalling—such as activation of TRPA1—attenuate the fibrotic response and reduce SCI-induced bladder fibrosis in vivo [37]. Inflammatory signalling converges on the same outcome: activation of the NF-κB pathway and epithelial pyroptosis have been shown to promote neurogenic bladder fibrosis, and their inhibition is protective in experimental models [38]. Table 4 summarises the principal molecular mediators and their morphofunctional effects.

Mediator / pathway	Main source / trigger	Morphofunctional effect	Sources
NGF (neurotrophin)	Bladder wall & cord after obstruction/hypertrophy	C-fibre sensitisation, ↑TRPV1, afferent hypertrophy → NDO, DSD, dysreflexia	[9,10,28,30,31,74]
TGF-β1 / Smad	Mechanical strain, macrophages, inflammation	Myofibroblast activation, ↑collagen I/III & fibronectin → fibrosis, ↓compliance	[37,39]
NF-κB / pyroptosis	Inflammatory signalling in urothelium	Epithelial injury, pro-fibrotic remodelling	[38]
TRP channels (TRPV1/TRPA1)	Urothelium & afferents	Altered mechano-/nociceptive signalling; TRPA1 activation is anti-fibrotic	[10,37]
Axonal-growth regulators (CGRP, GAP-43, CSPGs)	Lumbosacral cord & DRG	Afferent sprouting paralleling NDO onset	[10,29]

Table 4. Principal molecular mediators of morphofunctional bladder remodelling after SCI. NGF, nerve growth factor; TGF-β1, transforming growth factor-β1; NDO, neurogenic detrusor overactivity; DSD, detrusor–sphincter dyssynergia; CSPGs, chondroitin sulphate proteoglycans.

3.7. Lesion-level and model-dependent differences

The morphofunctional phenotype is strongly dictated by the anatomical level and the mechanical nature of the lesion. Suprasacral injuries typically produce a hyperreflexic detrusor with NDO and, frequently, DSD- the constellation that carries the highest risk of high pressure, low compliance, fibrosis, reflux and renal injury [5,6]. Lesions of the conus medullaris or mixed lesions combine upper- and lower-motor-neuron features and behave unpredictably, so that urodynamic characterisation is indispensable [5,6]. In contrast, sacral or infrasacral (cauda equina) lesions damage the sacral parasympathetic reflex arc itself; the detrusor is typically areflexic or acontractile with a flaccid outlet, and chronic retention with overflow incontinence predominates, while detrusor overactivity is reported in only a minority (approximately 15–31%) of cauda-equina cases [5,6].

The relative proportions of overactive versus underactive phenotypes by level are illustrated in Figure 6. Experimental model choice also matters: complete transection tends to produce an obstructive, high-pressure, high-threshold voiding pattern, whereas contusion injuries generate more uninhibited detrusor contractions and non-voiding hyperactivity, reflecting divergent neuroplastic processes and differing degrees of afferent sprouting [18,25]. These model-specific differences must be considered when translating experimental findings to patients.

Lesion localisation	Dominant bladder pattern	Key morphofunctional risk
Suprasacral SCI	Hyperreflexic detrusor, NDO, frequently DSD	High pressure, low compliance, fibrosis, reflux, renal injury
Conus / mixed lesion	Variable upper- and lower-motor-neuron features	Unpredictable detrusor & sphincter behaviour; urodynamics essential
Sacral / infrasacral (cauda equina)	Areflexic/acontractile hypotonic detrusor; flaccid sphincter	Chronic retention, overdistension, overflow incontinence, infection, stones

Table 5. Lesion-level differences in bladder phenotype and morphofunctional risk after SCI. NDO, neurogenic detrusor overactivity; DSD, detrusor–sphincter dyssynergia. Synthesised from [5,6,18,25].

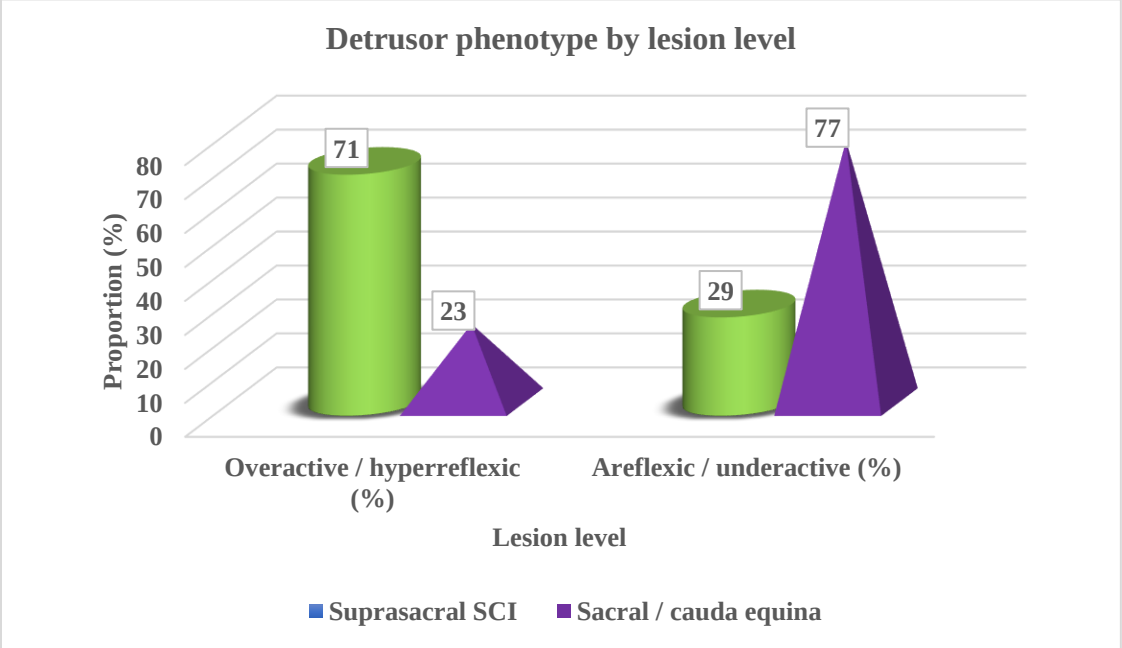

Figure 6. Detrusor phenotype distribution by lesion level

3.8. Framework for morphofunctional assessment

Because structure and function can dissociate, a morphofunctional investigation should interpret structural findings together with functional testing. A robust study design combines: (i) urodynamics—cystometric capacity, compliance, detrusor pressure, non-voiding contractions, leak-point pressure, post-void residual and evidence of DSD; (ii) imaging-ultrasonography for wall thickness, residual urine, hydronephrosis and hydroureter, with videourodynamics where reflux or outlet dysfunction is suspected; (iii) macromorphometry-bladder mass, bladder-to-body-weight ratio,

wall thickness, capacity, trabeculation and diverticula; (iv) routine histology (haematoxylin–eosin) for architecture and inflammation; (v) connective-tissue analysis-Masson trichrome or Sirius Red with quantitative collagen-area fraction and, where relevant, type I/III immunohistochemistry; (vi) muscular and neural markers—α-smooth-muscle actin, desmin, myosin heavy chain, S100, PGP9.5 and markers of afferents or mechanotransduction; and (vii) explicit functional–morphological correlations, for example wall thickness or collagen fraction versus compliance, maximum detrusor pressure, residual urine and voiding efficiency. Urodynamics is central to this scheme because it identifies poor compliance, DSD and high storage/voiding pressures-the "silent" risk factors for upper-tract damage—whereas ultrasound alone cannot distinguish a safe high-capacity bladder from a dangerous high-pressure reservoir [5,8].

4. Discussion

The evidence reviewed here converges on a coherent picture: the neurogenic bladder after SCI is not a fixed lesion but a staged morphofunctional continuum whose structural and functional characteristics change in a predictable, mechanistically linked sequence. An acute areflexic reservoir gives way to a subacute reflex-hyperactive organ and, in most suprasacral injuries, to a chronic high-pressure bladder with DSD; abnormal pressure and incomplete emptying then drive hypertrophy, neural and stromal remodelling, collagen accumulation and fibrosis [5,9,10,11]. Recognising which point of this continuum a given bladder occupies is more informative than any single static descriptor, and it reconciles findings that would otherwise appear contradictory.

4.1. Reconciling divergent structural and functional findings

Two apparent paradoxes in the literature are resolved by a stage- and organisation-aware reading. First, wall thickening and hypertrophy are frequently equated with a "stronger" bladder, yet the same thickening reflects, at later stages, the replacement of contractile muscle by non-contractile matrix; contractile performance falls not because individual myocytes fail but because detrusor mass is progressively diluted by ECM [21,34]. This is why a thick, trabeculated wall on imaging cannot be assumed to be functionally competent. Second, chronic SCI has been reported to produce both stiff, low-compliance bladders and, in a subset, paradoxically compliant, underactive bladders. The biomechanical time-course data explain this: compliance rises transiently in the early weeks and only later declines as mature fibrosis and a type III→I collagen shift stiffen the wall, while altered collagen-fibre waviness can delay fibre recruitment and mimic increased compliance [19,21,36]. The direction of the final phenotype thus depends on the amount, isoform balance and spatial organisation of deposited matrix, not merely on its presence.

4.2. Mechanistic coherence: a self-reinforcing loop

The molecular data provide a unifying mechanism. DSD and outlet resistance generate high intravesical pressure and incomplete emptying; the resulting hypertrophy and wall stress raise NGF, which sensitises C-fibre afferents and intensifies NDO, further raising pressure; simultaneously, mechanical strain and inflammation activate TGF-β1/Smad and NF-κB signalling, converting fibroblasts to matrix-producing myofibroblasts and depositing stiff collagen that lowers compliance and worsens emptying [9,10,37,38,39]. This feed-forward loop links the functional and structural arms of the disease and explains why early, pressure-lowering intervention is so consistently protective in experimental work—for example, early detrusor chemodenervation limits hypertrophy and fibrosis [20], and early neuromodulation preserves afferent quiescence and prevents detrusor overactivity. The loop also identifies rational molecular targets (NGF neutralisation, TGF-β/Smad or NF-κB inhibition, TRPA1 activation), several of which reduce fibrosis or overactivity in preclinical models [30,31,37,38].

4.3. Clinical implications

Three implications follow for practice. First, the most dangerous phenotype—the chronic suprasacral, high-pressure, low-compliance bladder with DSD—must be identified before it damages the upper tract; a detrusor pressure exceeding roughly 40 cm H_2O remains a practical alarm threshold [8,45]. Second, because the phenotype evolves, a single early assessment is insufficient; repeated urodynamic surveillance is needed to track the transition from areflexia to NDO/DSD and to detect declining compliance, and it should guide bladder management aimed at maintaining low-pressure storage and efficient emptying [5,6,8]. Third, the window during which remodelling is still reversible appears to be early: the preclinical protection afforded by early pressure-lowering interventions argues for prompt, proactive management rather than reaction to established complications [20]. The staged model thus supports a strategy of early risk stratification and upper-tract-protective management individualised by lesion level and urodynamic phenotype.

4.4. Gaps and future directions

Several gaps limit current understanding. Much mechanistic and morphometric evidence derives from rodent transection models, whose tempo and phenotype differ from

human contusion injuries; large-animal (minipig) and well-characterised human tissue studies remain comparatively scarce [19,25]. The temporal mapping between molecular events (NGF and TGF-β dynamics), afferent plasticity and quantitative histological change is incompletely resolved, and standardised, quantitative morphofunctional end points-collagen-area fraction, muscle-to-collagen ratio, type I/III ratio, wall thickness-are inconsistently reported, hampering meta-analysis. Future work should therefore prioritise: harmonised, operationally defined staging that couples time after injury with urodynamic criteria; longitudinal designs that pair serial urodynamics with sequential histology and molecular profiling; validated non-invasive biomarkers or imaging surrogates of wall fibrosis; and rigorously timed trials of anti-remodelling therapies. Emerging regenerative and circuit-restorative strategies-stem-cell approaches, neuromodulation and tissue engineering-will require exactly this kind of morphofunctional read-out to demonstrate that they restore function and not merely structure [26,40,41].

4.5. Limitations of this review

This is a narrative review and is subject to selection and language bias; it did not follow a formal systematic-review protocol and did not perform quantitative synthesis, which was precluded by heterogeneity of species, injury models, severity and time points. The quantitative values presented are illustrative of direction and magnitude rather than pooled estimates, and cross-species extrapolation should be made cautiously. Nonetheless, the convergence of independent human and experimental lines of evidence lends confidence to the central conclusion of a staged morphofunctional continuum.

5. Conclusion

The urinary bladder after spinal cord injury undergoes a reproducible, time-dependent morphofunctional evolution. From an acute areflexic, retentive reservoir during spinal shock, it progresses through a subacute phase of neurogenic detrusor overactivity—driven by NGF-dependent C-fibre afferent sprouting—to a chronic phase, most consequentially after suprasacral lesions, characterised by detrusor–sphincter dyssynergia, smooth-muscle hypertrophy, extracellular-matrix accumulation with a type III→I collagen shift and elastin loss, and ultimately fibrosis with reduced compliance and contractility. Sacral and infrasacral lesions more often yield an acontractile, large-capacity retention bladder. Because wall thickening does not equate to preserved function, structural findings must always be interpreted together with urodynamics. The chronic suprasacral high-pressure, low-compliance bladder with DSD is the phenotype most threatening to the upper urinary tract and the principal target of early, individualised, upper-tract-protective management. A staged, mechanistically grounded morphofunctional framework should guide both clinical surveillance and future translational research.

Declarations

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References

1. Lu Y, Shang Z, Zhang W, Pang M, Hu X, Dai Y, et al. Global incidence and characteristics of spinal cord injury since 2000–2021: a systematic review and meta-analysis. BMC Med. 2024;22(1):285.
2. GBD 2019 Spinal Cord Injuries Collaborators. Global, regional, and national burden of spinal cord injury, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2023;22(11):1026–1047.
3. Ding W, Hu S, Wang P, Kang H, Peng R, Dong Y, et al. Spinal cord injury: the global incidence, prevalence, and disability from the Global Burden of Disease Study 2019. Spine (Phila Pa 1976). 2022;47(21):1532–1540.
4. Kang Y, Ding H, Zhou H, Wei Z, Liu L, Pan D, et al. Epidemiology of worldwide spinal cord injury: a literature review. J Neurorestoratol. 2018;6:1–9.
5. Hamid R, Averbeck MA, Chiang H, Garcia A, Mousa RAT, Oh SJ, et al. Epidemiology and pathophysiology of neurogenic bladder after spinal cord injury. World J Urol. 2018;36(10):1517–1527.
6. Al Taweel W, Seyam R. Neurogenic bladder in spinal cord injury patients. Res Rep Urol. 2015;7:85–99.
7. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. Nat Rev Neurosci. 2008;9(6):453–466.
8. Panicker JN, Fowler CJ, Kessler TM. Lower urinary tract dysfunction in the neurological patient: clinical assessment and management. Lancet Neurol. 2015;14(7):720–732.
9. de Groat WC, Yoshimura N. Plasticity in reflex pathways to the lower urinary tract following spinal cord injury. Exp Neurol. 2012;235(1):123–132.
10. Shimizu N, Saito T, Wada N, Hashimoto M, Shimizu T, Kwon J, et al. Molecular mechanisms of neurogenic lower urinary tract dysfunction after spinal cord injury. Int J Mol Sci. 2023;24(9):7885.

11. Wada N, Karnup S, Kadekawa K, Shimizu N, Kwon J, Shimizu T, et al. Current knowledge and novel frontiers in lower urinary tract dysfunction after spinal cord injury: basic research perspectives. Urol Sci. 2022;33(3):101–113.
12. Kozomara M, Birkhäuser V, Anderson CE, Bywater M, Gross O, Kiss S, et al. Neurogenic lower urinary tract dysfunction in the first year after spinal cord injury: a descriptive study of urodynamic findings. J Urol. 2023;209(1):225–232.
13. Kim O, An L, Lee BC. Urodynamic evaluation of neurogenic bladder in patients with spinal cord injury within 6 months post-injury: a retrospective cross-sectional study. Spinal Cord. 2025;63(5):246–251.
14. Hogg FRA, Kearney S, Solomon E, Gallagher MJ, Zoumprouli A, Papadopoulos MC, et al. Acute, severe traumatic spinal cord injury: improving urinary bladder function by optimizing spinal cord perfusion. J Neurosurg Spine. 2021;35(6):1–8.
15. Mimata H, Satoh F, Tanigawa T, Nomura Y, Ogata J. Changes of rat urinary bladder during the acute phase of spinal cord injury. Urol Int. 1993;51(2):89–93.
16. Herrera JJ, Haywood-Watson RJ 2nd, Grill RJ. Acute and chronic deficits in the urinary bladder after spinal contusion injury in the adult rat. J Neurotrauma. 2010;27(2):423–431.
17. Sartori AM, Hofer AS, Scheuber MI, Rust R, Kessler TM, Schwab ME. Slow development of bladder malfunction parallels spinal cord fiber sprouting and interneurons' loss after spinal cord transection. Exp Neurol. 2021;348:113937.
18. Breyer BN, Fandel TM, Alwaal A, Osterberg EC, Shindel AW, Lin G, et al. Comparison of spinal cord contusion and transection: functional and histological changes in the rat urinary bladder. BJU Int. 2017;119(2):333–341.
19. Foditsch EE, Roider K, Patras I, Huțu I, Bauer S, Janetschek G, et al. Structural changes of the urinary bladder after chronic complete spinal cord injury in minipigs. Int Neurourol J. 2017;21(1):12–19.
20. Bushnell J, Cates LN, Hyde J, Hofstetter CP, Yang CC, Khaing ZZ. Early detrusor application of botulinum toxin A results in reduced bladder hypertrophy and fibrosis after spinal cord injury in a rodent model. Toxins. 2022;14(11):777.
21. Tuttle TG, Lujan HL, Tykocki NR, DiCarlo SE, Roccabianca S. Remodeling of extracellular matrix in the urinary bladder of paraplegic rats results in increased compliance and delayed fiber recruitment 16 weeks after spinal cord injury. Acta Biomater. 2022;141:280–289.
22. Von Siebenthal M, Akshay A, Besic M, Schneider MP, Gheinani AH, Burkhard FC, et al. Molecular characterization of non-neurogenic and neurogenic lower urinary tract dysfunction in SCI-induced and partial bladder outlet obstruction mouse models. Int J Mol Sci. 2023;24(3):2451.
23. Bai K, Hou Y, Zhang Z, Yuan F, Huang X, Liu P, et al. A new rat model of sacral cord injury producing a neurogenic bladder and its functional and mechanistic studies. Biomolecules. 2024;14(9):1141.
24. Ferreira A, Chambel SS, Avelino A, Cruz CD. Spinal cord injury causes marked tissue rearrangement in the urethra—an experimental study in the rat. Int J Mol Sci. 2022;23(24):15951.
25. Ferreira A, Chambel SS, Avelino A, Nascimento D, Silva N, Duarte Cruz C. Urinary dysfunction after spinal cord injury: comparing outcomes after thoracic spinal transection and contusion in the rat. Neuroscience. 2024;554:70–81.
26. Li J, Huang J, Chen L, Ren W, Cai W. Human umbilical cord mesenchymal stem cells contribute to the reconstruction of bladder function after acute spinal cord injury via the p38 MAPK/NF-κB pathway. Bioengineered. 2022;13(2):4844–4856.
27. Yoshimura N, de Groat WC. Effects of spinal cord injury on neurofilament immunoreactivity and capsaicin sensitivity in rat dorsal root ganglion neurons innervating the urinary bladder. Neuroscience. 1998;83(2):633–643.
28. Zvara P, Vizzard MA. Exogenous overexpression of nerve growth factor in the urinary bladder produces bladder overactivity and altered micturition circuitry in the lumbosacral spinal cord. BMC Physiol. 2007;7:9.
29. Chambel SS, Ferreira A, Oliveira R, Miranda R, Vale L, Reguenga C, et al. Development of neurogenic detrusor overactivity after thoracic spinal cord injury is accompanied by time-dependent changes in lumbosacral expression of axonal growth regulators. Int J Mol Sci. 2022;23(15):8667.
30. Seki S, Sasaki K, Fraser MO, Igawa Y, Nishizawa O, Chancellor MB, et al. Immunoneutralization of nerve growth factor in lumbosacral spinal cord reduces bladder hyperreflexia in spinal cord injured rats. J Urol. 2002;168(5):2269–2274.
31. Seki S, Sasaki K, Igawa Y, Nishizawa O, Chancellor MB, de Groat WC, et al. Suppression of detrusor–sphincter dyssynergia by immunoneutralization of nerve growth factor in lumbosacral spinal cord in spinal cord injured rats. J Urol. 2004;171(1):478–482.
32. Ochodnicky P, Cruz CD, Yoshimura N, Cruz F. Neurotrophins as regulators of urinary bladder function. Nat Rev Urol. 2012;9(11):628–637.
33. Cruz CD. Neurotrophins in bladder function: what do we know and where do we go from here? Neurourol Urodyn. 2014;33(1):39–45.

34. Fry CH, Kitney DG, Paniker J, Drake MJ, Kanai A, Andersson KE. Fibrosis and the bladder, implications for function. ICI-RS 2017. Neurourol Urodyn. 2018;37(S4):S7–S12.

35. Johnston L, Cunningham RM, Young JS, Fry CH, McMurray G, Eccles R, et al. Altered distribution of interstitial cells and innervation in the rat urinary bladder following spinal cord injury. J Cell Mol Med. 2012;16(7):1533–1543.

36. Toosi KK, Nagatomi J, Chancellor MB, Sacks MS. The effects of long-term spinal cord injury on the mechanical properties of the rat urinary bladder. Ann Biomed Eng. 2008;36(9):1470–1480.

37. Zhao M, Ding N, Wang H, Zu S, Liu H, Wen J, et al. Activation of TRPA1 in bladder suburothelial myofibroblasts counteracts TGF-β1-induced fibrotic changes. Int J Mol Sci. 2023;24(11):9501.

38. Chen J, Li Q, Hong Y, Zhou X, Yu C, Tian X, et al. Inhibition of the NF-κB signaling pathway alleviates pyroptosis in bladder epithelial cells and neurogenic bladder fibrosis. Int J Mol Sci. 2023;24(13):11160.

39. Yang X, Pu Q, Wen Y, Zhao Y, Wang J, Xu P, et al. Activation of the TGF-β1/Smads/α-SMA pathway is related to histological and functional changes in children with neurogenic bladder. Sci Rep. 2022;12:9631.

40. Steadman CJ, Grill WM. Spinal cord stimulation for the restoration of bladder function after spinal cord injury. Healthc Technol Lett. 2020;7(3):87–92.

41. Chen SF, Jiang YH, Jhang JF, Kuo HC. Satisfaction with detrusor onabotulinumtoxinA injections and conversion to other bladder management in patients with chronic spinal cord injury. Toxins. 2022;14(1):35.

42. Cameron AP, Wallner LP, Tate DG, Sarma AV, Rodriguez GM, Clemens JQ. Bladder management after spinal cord injury in the United States 1972 to 2005. J Urol. 2010;184(1):213–217.

43. Weld KJ, Dmochowski RR. Effect of bladder management on urological complications in spinal cord injured patients. J Urol. 2000;163(3):768–772.

44. Gerridzen RG, Thijssen AM, Dehoux E. Risk factors for upper tract deterioration in chronic spinal cord injury patients. J Urol. 1992;147(2):416–418.

45. McGuire EJ, Woodside JR, Borden TA, Weiss RM. Prognostic value of urodynamic testing in myelodysplastic patients. J Urol. 1981;126(2):205–209.

46. Ruffion A, Castro-Díaz D, Patel H, Khalaf K, Onyenwenyi A, Globe D, et al. Systematic review of the epidemiology of urinary incontinence and detrusor overactivity among patients with neurogenic overactive bladder. Neuroepidemiology. 2013;41(3-4):146–155.

47. Wyndaele JJ. The management of neurogenic lower urinary tract dysfunction after spinal cord injury. Nat Rev Urol. 2016;13(12):705–714.

48. Manack A, Motsko SP, Haag-Molkenteller C, Ruggieri M, Chancellor MB, Sahai A, et al. Epidemiology and healthcare utilization of neurogenic bladder patients in a US claims database. Neurourol Urodyn. 2011;30(3):395–401.

49. Kaplan SA, Chancellor MB, Blaivas JG. Bladder and sphincter behavior in patients with spinal cord lesions. J Urol. 1991;146(1):113–117.

50. Groen J, Pannek J, Castro Diaz D, Del Popolo G, Gross T, Hamid R, et al. Summary of European Association of Urology (EAU) guidelines on neuro-urology. Eur Urol. 2016;69(2):324–333.

51. Drake MJ, Apostolidis A, Cocci A, Emmanuel A, Gajewski JB, Harrison SCW, et al. Neurogenic lower urinary tract dysfunction: clinical management recommendations of the Neurologic Incontinence Committee of the Fifth International Consultation on Incontinence 2013. Neurourol Urodyn. 2016;35(6):657–665.

52. Vizzard MA. Neurochemical plasticity and the role of neurotrophic factors in bladder reflex pathways after spinal cord injury. Prog Brain Res. 2006;152:97–115.

53. Kadekawa K, Yoshimura N, Majima T, Wada N, Shimizu T, Birder LA, et al. Characterization of bladder and external urethral activity in mice with or without spinal cord injury—a comparison study with rats. Am J Physiol Regul Integr Comp Physiol. 2016;310(8):R752–R758.

54. Andersson KE, Wein AJ. Pharmacology of the lower urinary tract: basis for current and future treatments of urinary incontinence. Pharmacol Rev. 2004;56(4):581–631.