FEMALE UROLOGY (L COX, SECTION EDITOR)

Knowledge Gaps in Urologic Care of Female Spinal Cord Injury Patients

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Abstract

Purpose of Review We highlight the substantial gaps in knowledge on urologic care of female spinal cord injury (SCI) patients.

Recent Findings Males account for approximately 80% of people living with SCI in developed nations. Although there is a robust body of literature in some aspects of urologic care of individuals with SCI, such as treatments for neurogenic detrusor overactivity, there are relatively few studies focusing specifically on females. There are also few studies focusing on other aspects of urologic care of women with SCI such as sexual dysfunction, pelvic organ prolapse, and bladder cancer. Established guidelines for bladder management exist, generally recommending intermittent catheterization, but the fact remains that a substantial number of women with SCI utilize indwelling catheters for bladder management. There remains a paucity of literature using patient-reported measures regarding both outcomes and experiences of urologic management in the SCI population.

Summary Bladder management is challenging for many women with SCI. There are few studies on other urologic concerns in women with SCI.

Keywords Female · Spinal cord injury · Urologic management

Introduction

Lower urinary tract dysfunction associated with spinal cord injury (SCI) may profoundly impact on health and well-being. Urologic management of the individual with spinal cord injury (SCI) is complex with significant medical, social, and economic implications. Although many organizations have issued guidelines on the evaluation and treatment of neurogenic lower urinary tract dysfunction, there are substantial gaps in knowledge of management for female SCI patients due to a scarcity of high-quality research [1–3]. There are clear differences between men and women with SCI in the cause of injury, prevalence, medication usage, and use of personal attendants, and type of health insurance coverage [4]. It is clear that urologic care of women with SCI is hampered by multiple knowledge gaps including intervention for neurogenic lower

urinary tract dysfunction, sexual dysfunction, pelvic organ prolapses, and patient-reported outcomes research.

Epidemiology

Spinal cord injury (SCI) is associated with numerous life-threatening complications and carries substantial permanent psychologic, social, and economic consequences. The World Health Organization estimates that 250,000 to 500,000 new spinal cord injuries occur annually [5]. Estimations of the global prevalence of SCI have been hampered by missing data on prevalence and non-standardized reporting throughout much of the world, particularly in developing countries. While there is apparent regional variance in the incidence and prevalence of SCI, most systematic reviews have been undertaken in developed countries.

The National Spinal Cord Injury Statistical Center, using data from the Spinal Cord Injury (SCI) Model System, estimates that there are currently about 288,000 people living with spinal cord injury in the USA [6]. It is projected that there will be 17,700 new cases of SCI this year in the USA, with approximately 78% of these injuries occurring in males. This projection is consistent with historical data indicating that only

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about 20% of people living with SCI are female. Multiple studies worldwide also consistently show a much higher incidence of adult spinal cord injury among males.

The age of spinal cord injury has increased over the past several decades and now has a bimodal distribution with one peak in young adults, and the other occurring at ages greater than 60 [7, 8]. The higher rate of spinal cord injury in young adults has been associated with alcohol use, unsafe driving behaviors, and participation in sports with a higher risk of injury. The increased incidence of spinal cord injury in person over 60 years of age probably reflects the higher rate of falls from standing height in older individuals, though this requires further study. The proportion of SCI suffered in the elderly is more evenly distributed between male and female. Demographic shifts in developed countries will likely result in an increasing number of the elderly, and females, with SCI. It is likely that the second peak, particularly females with cervical central cord injuries, will grow.

Mortality

Historically, renal and urologic causes were the most prominent cause of mortality in patients with chronic SCI. A recent study conducted by Savic and colleagues included over 5000 patients with spinal cord injuries suffered between 1943 and 2010 [9•]. The study sought to analyze the leading causes of mortality after the first year post-injury. The data showed the leading causes of death were attributed to: respiratory (29.3%), cardiovascular/cerebrovascular (26.7%), neoplasms (13.9%), urogenital (11.5%), and digestive complications (5.3%). Urinary tract infections were the most frequently reported cause of death among patients with a urogenital source of mortality. The same study, when sub-stratified by period, demonstrated that urogenital-related causes accounted for 32.8% of deaths during the period from 1944 to 1969. In subsequent time periods, the rates of urogenital causes of death declined. While urologic management has undoubtedly improved over the past 50 years, it is likely that advances in the treatment of urinary tract infections and septicemia most likely accounts for the majority of the drop in urogenital deaths.

This study also highlights that SCI patients are more likely to develop bladder cancer. A review of cancer diagnoses among the study population indicated that bladder cancer accounted for 9.6% of all cancers. In comparison to general population prevalence rates, the study determined that SCI patients have a 14% higher overall cancer prevalence rate.

These results are consistent with other published findings in the SCI literature. One study showed that patients with SCI were 6.7 times more likely to die from bladder cancer than the general population when controlled for age, gender, and race/ethnicity [10•]. These results come from a study including over 45,000 patients treated within the US Spinal Cord Injury Model System or at Shriners Hospital. This study also found significantly higher mortality in females than males, with a standardized mortality ratio of 12.21 in females versus 5.96 in males. The authors postulated that this result was likely related to the findings in multiple studies that females with SCI more commonly use indwelling catheters compared to male SCI patients. Although the SCI population is clearly at higher risk to both develop and die from bladder cancer, there is currently no high-quality evidence that supports regular screening for bladder cancer in asymptomatic SCI individuals. While routine cystoscopic examinations have been reported to identify asymptomatic bladder cancers, there is no evidence that a structured screening program can result in earlier detection, which in turn leads to lower cancer-specific death rates [11]. It appears that a relatively low incidence rate, combined with the typically aggressive progression of cancer in SCI patients, means that cystoscopy and bladder biopsy are not able to be well evaluated in these studies, and therefore did not fulfill the criteria for a screening test due.

Although an association between bladder cancers in SCI has been described for over 50 years, it is taking on greater importance as the long-term survival of SCI individuals has improved [12–15]. Proposed factors which predispose patients with SCI to bladder cancer include neurogenic factors, long-term indwelling catheter use, infectious complications, and urinary stasis. We do not currently recommend screening for bladder cancer in patients with SCI, but favor a low threshold for endoscopic evaluation, particularly in chronically catheterized patients.

Bladder Outlet Dysfunction

Urinary incontinence continues to be common in women with SCI and is associated with reduced quality of life in general, physical, and emotional domains [16]. Management strategies for neurogenic detrusor overactivity (NDO) and urgency urinary incontinence (UUI), such as intradetrusor onabotulinumtoxin A and augmentation cystoplasty, are generally accepted and often supported by relatively high-quality evidence.

Unfortunately, many women with SCI also experience urinary incontinence resulting from intrinsic sphincteric deficiency (ISD), which frequently coexists with NDO. There are many approaches to correct incontinence related to ISD in women with SCI, including periurethral bulking, suburethral slings, bladder neck slings, bladder neck reconstruction, and artificial sphincters. However, the current literature lacks robust data to devise a treatment algorithm for stress urinary incontinence (SUI) in female SCI patients or to help predict treatment outcomes for these patients. Much of the published

literature about SUI in neurogenic subjects comes from studies in children with myelomeningoceles, in whom outlet incompetence is more common than in individuals with SCI.

Endoscopic periurethral bulking procedures improve continence by increasing outflow resistance in patients with urinary incontinence due to dysfunction or denervation of the urinary sphincter. Various injectable materials have been used including polytetrafluoroethylene, glutaraldehyde cross-linked bovine collagen (GAX), dextranomer microspheres (Deflux®), calcium hydroxylapatite (Coaptite®), and polydimethylsiloxane (Macroplastique®). A small study of six female patients with neurogenic ISD treated with polytetrafluoroethylene reported complete continence when combined with intermittent catheterization [17]. One study of 11 patients treated with periurethral GAX showed cure or significant improvement in seven patients, while four were reported as only slightly improved or no better [18]. Bulking has also been studied in the setting of a failed fascial sling in children with ISD and neurogenic bladder dysfunction. With a median follow-up of 8 years, only two of the 27 patients were continent, despite repeat injections in many participants [19]. The available literature is characterized by small sample size, variable interventions, and variable outcomes. Despite this lack of relevant data, we utilize periurethral bulking in our practice either as a first line SUI procedure or as an adjuvant intervention after a sling procedure has failed.

For female SCI patients with SUI, the pubovaginal sling (PVS) has gained widespread use as a durable and reliable means in which to increase bladder outlet resistance by providing support to the bladder neck and proximal urethra [20]. These slings can be fashioned from autologous fascia, an allograft, or a xenograft. This sling can be fashioned to allow urethral compression if necessary in women with severe ISD. Even when PVS have been positioned to provide bladder neck and proximal urethra compression, PVS remain associated with low rates of urethral erosion, vaginal erosion, and local tissue reaction. In contrast to synthetic slings, PVS can be placed in patients on intermittent catheterization without significant concern for additional long-term urethral trauma and complications. The concept of fashioning a fascial sling under greater tension to achieve functional urethral closure in women with a devastated urethra resulting from long-term urethral catheterization has been reported to have excellent results [21].

Although the evidence for PVS repair remains limited in the neurogenic adult population compared to the pediatric literature, several small studies have reported positive outcomes. One study of 33 female patients undergoing autologous sling placement, including 12 with SCI, found that 76% were completely dry in the postoperative setting and 15% were markedly improved [22]. Overall, the women reported a 91% satisfaction rate. Women with neurogenic bladders and stress urinary incontinence have generally been found to have comparable results when compared to non-neurogenic women. A prospective study of 21 women with neurogenic bladder and ISD, including eight with spinal cord injury, treated each patient a combined rectus fascial sling and ileocystoplasty. The study reported that 95% of subjects were completely dry with the utilization of CIC [23].

More recent studies have explored the uses of a synthetic tension-free mid-urethral sling (MUS) to address SUI and ISD in female neurogenic patients. Unlike fascial slings, which generally result in the need for permanent intermittent catheterization, mid-urethral slings may allow voiding to achieve bladder emptying in patients not requiring intermittent catheterization. One study of 12 female patients with neurogenic bladder, including three with SCI, reported cure in 83.3% and improvement in 8.3%. All three patients voiding before the procedure were able to do so post-operatively, and no severe complications were reported [24].

A retrospective study of nine female patients with SCI who underwent trans-obturator sling (TOT) placement found improvement in only 33%, with one late urethral erosion noted [25]. Another retrospective review of 27 female neurogenic patients undergoing TOT placement reported a cure rate of 81.5% following surgery [26]. Similar favorable results were published in a trial of 12 women with SCI and SUI who were treated with placement of a retropubic MUS [27].

A more recent study examined the placement of either a retropubic MUS or a TOT sling in female SCI patients. Quality of life was improved in 52.6% and 68.4%, respectively [28]. Nine patients developed MUS-related complications, including five with de novo urgency, one with frequent dysreflexia require sling incision, and one with vaginal mesh extrusion. Concomitant procedures were often performed, including the use of botulinum toxin in 46.6% and augmentation cystoplasty in 10% of these patients. Although the vaginal extrusion rate was low in this study and no urethral erosions were reported, the use of mesh slings in women with SCI should be approached with great caution until larger studies with longer-term outcomes are reported.

Similar to periurethral bulking and sling placement, the role of the artificial urinary sphincters (AUS) in female SCI patients is not well characterized. Results appear to be poor when compared to PVS and seem to be associated with higher rates of failure, as defined by the need for re-operation [29]. The use of the AUS to treat ISD in female SCI patients should be reserved for only in highly selected cases.

Female SCI patients may also present with SUI/ISD secondary to urethral erosion. In cases of urethral loss, but maintenance of adequate bladder capacity, our practice is to perform a transvaginal bladder neck closure and simultaneous creation of an alternate means for bladder drainage [30]. In severe cases of bladder neck compromise in a setting of a very small capacity bladder, we will consider a urinary diversion.

The management of SUI in women with SCI is further complicated by concomitant neurogenic bladder dysfunction. Confusing the matter is that most studies are observational in the SCI population and are confounded by concomitant procedures, usually enterocystoplasty, and subject heterogeneity resulting in a high likelihood of selection bias. Reporting and management guidelines are needed to aid in the management of ISD in this population.

Sexual Dysfunction

Due to the male preponderance of SCI, it is not surprising that relatively less attention has been focused on issues related to sexual function and dysfunction in women with SCI.

Physical limitations resulting from SCI effects are common, including changes in sexual activity for both males and females. Reduced sensation, spasticity, alterations in vaginal lubrication, and changes in orgasmic function are common physical challenges to sexual activity in women with SCI [31]. Other indirect factors, such as autonomic dysreflexia, pain, the presence of a urinary catheter, urinary and fecal incontinence, and side effects of medications also contribute to the challenges that these individuals face. Depression and feeling of altered body image are also frequently experienced by women with SCI [32].

While significant changes in sexual function, including alterations in genital sensitivity, physical responses to sexual arousal, vaginal lubrication, and orgasm are common in SCI, most women remain sexually active after a SCI [33–35]. It is crucial to understand the changes in sexual function that result and aid these women in optimizing and maximizing their sexual function, which has profound implications on quality of life [36, 37].

Sexual function remains possible regardless of SCI level. Normal sexual response is achievable in these patients, with some responding to psychogenic stimulation and others responding to reflexogenic or genital stimulation [38, 39]. The significant difference seems to be the level of spinal cord injury, as these different types of stimulation appear to be mediated through different neurological pathways. The ability to orgasm in women with SCI is often preserved, with 55% of women with SCI self-reporting the ability to orgasm whether through clitoral, genital, or cervical stimulation [38, 40]. Orgasm remains possible as these areas utilize different neural pathways, with the clitoris using somatosensory innervation, the vagina and cervix using parasympathetic innervation, and the cervix and uterus having sympathetic innervation [41, 42]. One study also assessed the level of injury, which does appear to play a role in the ability to achieve orgasm. Only 17% of women with complete lower motor neuron injuries involving the S2–S5 segments were able to reach orgasm compared to 59% of all other SCI female patients.

Assessment should include testing dermatomes and sensitivities of the clitoris, labia, vaginal entry, and anal sphincter [39]. Documentation can be standardized using the standards set up by the International Spinal Cord Injury Female Sexual Function Basic Data Set [43]. Once completed, rehabilitation can be offered for those interested. Vital in this rehabilitation is self-exploration, including stimulation of a variety of areas to see where sensation remains, though coaching is available if required. Additional goals of rehabilitation are to help with other problems that may pose a barrier to normal sexual function. These issues can include limited mobility, muscle contractures, concern with incontinence, as well as psychological barriers. Rehabilitation offers a variety of options to help combat these issues which, though not directly related to sexual function, certainly play a role in limiting female SCI patients' normal sexual functioning.

Similar to the erectile response in men, multiple pathways control vaginal lubrication in the brain and spinal cord, which may be affected by spinal cord injury. Vaginal lubrication from genital stimulation may be achieved in SCI women through intact sacral segments but the response, like reflexogenic erections in male, is often limited in duration and perceived as unsatisfactory. Anticholinergic medications are commonly used to manage incontinence but may contribute to dryness of the vagina.

Selective phosphodiesterase (PDE) inhibitors, such as sildenafil, vardenafil, and tadalafil have been successfully introduced in the oral treatment of male erectile dysfunction. Diminished vaginal lubrication can be addressed by using water-soluble lubricants, but in select individuals, PDE-5 inhibitors such as sildenafil may have a role [44]. PDE-5 inhibitors have been studied in only a few trials in the treatment of women with sexual dysfunction secondary to neurologic disease. Data is limited and clinical studies of this class in female sexual dysfunction suggest at best a limited role [45–47]. One small study of 19 women with multiple sclerosis showed improvement in vaginal lubrication, but not in other domains of sexual function. Clinicians may consider using PDE inhibitors in individual patients, but there are no evidence-based guidelines to suggest which patients may benefit the most from this class of medications.

The 5-HT 1A receptor agonist flibanserin is used for female hypoactive sexual desire disorder (HSDD), a condition characterized by a reduced desire for sexual activity that causes marked distress or interpersonal difficulty and is not accounted for by medications, relationship difficulties, or coexisting medical conditions. Although flibanserin has been proposed as a possible treatment for women with SCI associated with low sexual desire [48, 49], there are no studies in the SCI population that support its use.

Beyond medications, vibratory stimulation and clitoral vacuum suction devices have been studied for their ability to improve sexual function [50, 51]. There is limited data on

these techniques, particularly in SCI patients, and it is unclear what role they may play moving forward. Studies have shown both to be effective, with most considering vibratory stimulation a first line option and clitoral vacuum suction secondary. Although these modalities are available to women, further research is needed to examine satisfaction with these devices.

While sexual rehabilitation is a goal for many women with SCI that assumes much greater importance after initial rehabilitation is complete, the topic should be addressed as soon as is practical after initial SCI by an experienced medical professional. Interdisciplinary care may include referrals to professionals knowledgeable about spinal cord injury related to sexuality such as counselors for relationship issues and gynecologists for fertility concerns.

Pelvic Organ Prolapse

Pelvic organ prolapse (POP) is the abnormal descent of standard anatomic sites in the pelvis and may involve the uterus, vaginal apex, bladder, or bowel toward or through the vaginal introitus. Despite the high prevalence of pelvic organ prolapse in the general female population, there is limited knowledge about the prevalence and management of POP in female SCI patients. While there is a single case report implicating SCI as the primary factor in the development of POP after SCI, the authors postulate that this is due to peripheral atrophy resulted in the relaxation of the uterine suspension structures combined with pelvic floor muscle relaxation and weakness of the central perineal tendon [52]. No mention is made of the level of the injury in this paraplegic patient, nor is the method of bowel management described, which could undoubtedly contribute due to chronic abdominal straining. One study of POP in 280 women with multiple sclerosis found that only 9% had anatomical POP stage ≥ 2 [53•]. The authors suggested that women with a neurological disorder may have a lower prevalence of POP than neurologically intact women, possibly due to reduced physical activity with subsequent reduced physical stress on pelvic organs, pelvic connective tissues, and pelvic floor muscles. A more recent observational study of 98 women with SCI found that 21% had anatomical POP stage ≥ 2, with older age, postmenopausal status, parity, and previous vaginal delivery more common in those with POP [54]. This study noted no difference in duration, level, or completeness of injury among those with POP. The authors conclude that the prevalence of POP in women with SCI does not appear to be higher than in neurologically intact women.

As evidenced by the dearth of available literature focusing on female SCI patients, SCI alone has not been identified as an independent risk factor for developing clinically significant POP. When we encounter POP in our female SCI population, we approach our management options similarly to our nonneurogenic patients. Female SCI patients with POP are allowed to observe their POP and not intervene as long as their POP does not cause either urethral or rectal obstruction. Female SCI patients with a POP can also undergo management with the long term use of a pessary, or they can undergo a surgical repair. Clinical factors to consider when determining a treatment plan include their ability to maintain regular follow-up for pessary care and their ability to be placed in dorsal lithotomy for a transvaginal prolapse repair. A transabdominal prolapse repair may best serve female SCI patients with clinically significant POP who have challenging vaginal access.

Quality of Life and Patient-Reported Outcomes

Practice guidelines are a critical resource for practitioners but cannot account for every clinical scenario, are often not SCI-specific, and if applied rigidly may fail to weigh patient preference in management decisions successfully. The general preference by care providers is for the use of intermittent catheterization in SCI individuals. Individuals living with SCI, particularly women, often prefer the simplicity, convenience, and independence that indwelling catheters provide, which has led a large number of female SCI patients to have indwelling catheters. [55] Women with SCI appear to rate the difficulties with bladder management as a major disruptor of quality of life. [56••] The ultimate goal is to provide the best possible health and well-being outcomes for the patient with spinal cord injury according to her wishes, to enhance both her quality of life and participation in society.

There are vast challenges in including patient-reported measures regarding both outcomes and experiences of urologic complications of SCI. A disconnect exists between what care providers recommend and what individuals prefer, as is evident by the general lack in published patient-reported measures. While much is known regarding measurable medical outcomes of management strategies for neurogenic lower urinary tract dysfunction, patients often value their quality of life. To address the disconnect between what providers recommend and what patients experience with different management techniques has led to the creation of collaborative groups working to report patient-related outcomes in neurogenic bladder dysfunction. [57]

Well established therapies for neurogenic detrusor overactivity (NDO) include anticholinergics, medications intradetrusor onabotulinumtoxin A and surgical procedures, such as augmentation cystoplasty. [58] While few would argue that augmentation cystoplasty is the most effective intervention in treating NDO, there is only recent evidence that it is superior in terms of patient-reported satisfaction. Patients on intermittent catheterization with augmentation cystoplasty were more satisfied with lower urinary tract symptoms than those managed with intermittent

catheterization alone or with botulinum toxin. Multi-institution collaborations are critical for the generation of robust data and are vital to understanding the outcomes related to urologic management of women with SCI.

Conclusion

Although a substantial volume of research has been directed toward urologic care of women with spinal cord injury, many gaps remain. Female SCI urological care continues to be an area of concern, as there are significant deficiencies in knowledge which go unstudied, there is rampant duplication of research topics, and currently, relatively few interventions have a strong evidence base to support them.

Management of women with SCI is further hampered by the apparent focus on males in published studies. While this may be of limited importance in some areas, such as pharmacologic management of neurogenic detrusor overactivity, other domains of urologic concern to women with SCI, including sexual function, and pelvic organ prolapse are poorly studied.

Compliance with Ethical Standards

Conflict of Interest   Seth Teplitsky and Alana Murphy each declare no potential conflicts of interest.

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