ISCoS The International Spinal Cord Society

www.nature.com/scsandc

ARTICLE

Check for updates

Autologous fascial slings for stress urinary incontinence in patients with neuropathic bladder

A. Deytrikh[1,2]✉, A. P. Downey[1,2], A. Mangera[1,2] and S. V. Reid[1,2]

STUDY DESIGN: Retrospective review.
OBJECTIVES: Stress urinary incontinence in the neurogenic population can have a profound effect on quality of life. It can lead to significant skin breakdown and non-healing pressure sores. Surgical management options for stress incontinence include an autologous pubovaginal sling (PVS). We performed a retrospective review of female patients undergoing PVS insertion in a specialised unit to assess short-term efficacy and safety in this complex neurogenic population.
SETTING: Princess Royal Spinal Injuries Unit, Sheffield, UK.
METHODS: A retrospective review of all patients ($n = 22$) who had undergone insertion of a PVS was carried out in a single specialised spinal injury unit between 2015 to 2019. Patients were identified from a prospectively maintained database and from the electronic theatre records. Data was collected from the database, electronic patient records and radiological systems. All procedures were carried out by two experienced neurourology consultants.
RESULTS: The majority of patients were continent ($n = 19$, 86.4%) and 2 (13.5%) patients had an improvement in SUI following PVS insertion at a mean follow-up of 20 months. Pad use decreased from 5 to <1 and mean ICIQ-UI score improved from 17 to 1. One patient had a recurrence of stress urinary incontinence at 28 months. The median length of stay was three days. Three patients (13.6%) had a Clavien–Dindo Grade III–IV complication. One patient developed de-novo neurogenic detrusor overactivity.
CONCLUSION: The autologous PVS is a safe and efficacious procedure for the management of stress urinary incontinence in the neurogenic population with an acceptable morbidity and excellent short-term outcomes.

Spinal Cord Series and Cases (2022)8:25 ; https://doi.org/10.1038/s41394-022-00493-y

INTRODUCTION

Stress urinary incontinence (SUI) is a common condition with 20–30% of the female general population affected [1]. The types of conditions included in the term neurogenic population span a range of neurological aetiologies, including, spinal cord injuries, spina bifida, multiple sclerosis, and stroke. The incidence in the neurogenic population is unknown but presents a significant disabling symptom for these patients with a pronounced impact on their quality of life [1]. In addition, these patients can have significant baseline disability due to their underlying neurological condition that can predispose them to the development of pressure sores; in many cases healing can be delayed by significant incontinence and vice versa [2].

The pathophysiology of SUI in the neurogenic population can be broadly considered as three issues: intrinsic sphincter deficiency due to the underlying neurological condition, iatrogenic (e.g. due to long-term indwelling urethral catheter) or due to risk factors unrelated to the underlying neuropathy (e.g. parity, obesity etc). A combination of the above may also co-exist. Management can be more complicated as patients with neurogenic lower urinary tract dysfunction (NLUTD) may also have co-existing neurogenic detrusor overactivity (NDO) and low-compliant urinary bladders––it is extremely important that all women with NLUTD with SUI are assessed thoroughly to identify those with low compliance and therefore at higher risk of upper urinary tract damage. Patients with iatrogenic related SUI may have a significantly patulous urethra and should have the urethra and supporting tissue assessed at cystoscopy. The presence of poor supporting tissue, which could include urethral destruction due to catheter erosion, is unlikely to allow successful placement of a sling and may be predictive of a poor outcome from pubovaginal sling (PVS) insertion.

Conservative management options should always be considered as first-line treatment in any patient presenting with SUI however the appropriateness of pelvic floor muscle therapy should be considered on an individual patient basis as it may not be effective in many neurogenic patients due to underlying neurogenic pelvic floor dysfunction. Surgical options for treating SUI are bulking agents, mid-urethral synthetic slings, colposuspension, autologous PVS, insertion of artificial urinary sphincter and urethral closure, the latter necessitating the need for another means of bladder drainage (suprapubic catheter, mitrofanoff).

The pubovaginal fascial sling was first described by Giordano in 1907 but its widespread use for the treatment of stress urinary incontinence developed from the 1970's through the work of McGuire and Lytton [3]. Fascia is most commonly harvested from

[1]Princess Royal Spinal Injuries Unit, Sheffield, UK. [2]These authors contributed equally: Andrew Deytrikh, Alison Downey, Altaf Mangera, Sheilagh Reid.
✉email: andrew.deytrikh@nhs.net

Received: 14 October 2021 Revised: 4 February 2022 Accepted: 7 February 2022
Published online: 24 February 2022

the rectus sheath however fascia lata can also be utilised. The traditional goal of the sling is to produce increased bladder outlet resistance during episodes of increased intra-abdominal pressure while not causing obstruction during voluntary bladder emptying. The efficacy of the procedure is well established in the non-neurogenic population [4]. Complications include development of de novo NDO and urinary retention. However, it should be noted that many patients with NLUTD manage their bladders with catheterisation (either intermittent catheterisation or suprapubic catheter) and therefore it is not applicable in this cohort of patients. Current National Institute for Health and Care Excellence (NICE) guidelines recommend the use of autologous fascial slings for neurogenic SUI as first-line treatment [5] however, evidence for its specific use in adult female neurogenic patients is limited.

We performed a retrospective review of female patients with NLUTD in our unit undergoing autologous PVS insertion, using prospectively collected data to evaluate its efficacy and rate of complications.

MATERIALS AND METHODS

A retrospective review of all patients who had undergone insertion of a PVS was carried out in a single specialised spinal injury unit between 2015 and 2019. Twenty-two female patients were identified with a median age of 50 years (range 19–80). Three patients had previously failed procedures for SUI (two with colposuspension and one artificial urinary sphincter). One patient had a previous cystoplasty for neurogenic detrusor overactivity while sixteen patients were being treated for NDO prior to surgery with a variety of treatments including anticholinergics and intradetrusor botulinum toxin injections. All patients were counselled for the risk of retention post-operatively and those spontaneously voiding were taught ISC (Figs. 1–5).

Patients were identified from a prospectively maintained database and from the electronic theatre records. Data was collected from the database, electronic patient records and radiological systems. The patient demographics, neurological diagnosis and pre-operative catheter use is documented (Table 1). Pre-operative assessment included urinalysis, physical examination and flexible cystoscopy. All patients underwent urodynamics confirming SUI and an assessment was made of the compliance of the bladder to ensure safety at higher volumes, particularly in patients doing intermittent self-catheterisation (ISC). Urodynamics was performed in accordance with the International Continence Society guidelines, using a typical filling rate in this neurogenic population of 20 mls/min. This was done by occluding the urethral outlet and filling the bladder beyond the detrusor leak point pressure, to mimic an obstructive procedure on the bladder outlet.

All procedures were carried out in a similar procedure by two experienced neurourology consultants. A rectus fascia strip of 7–10 cm length and 2.5 cm width was harvested via a transverse suprapubic incision and 1–0 Ethilon sutures attached to either end of the fascia to create a “sling on a string”. A transverse incision is made in the anterior vaginal wall and a plane dissected laterally under the pubic bone. We then use an adapted McGuire needle which is passed from the abdominal incision into the vaginal incision (top-down approach) to position the sling.

Specifically, the suture is pulled through the needle to the suprapubic incision and tied at a later stage over the rectus fascia. This approach is preferred in our patient population due to the inherent difficulties in positioning these patients on the table due to muscular contractures.

A rigid cystoscopy is performed to assess for evidence of bladder perforation with needle withdrawal and repositioning if required. Tensioning was achieved with a 14Fr catheter in the bladder and the sutures tied over two fingers over the rectus sheath. Antibiotics were given from 24 h pre-operatively (guided by previous urine cultures) and orally for three days post-operatively. Patients with an indwelling suprapubic catheter have this changed at the start of the procedure during draping and prepping, and generally have the urethral catheter removed one day post-operatively. Those who are doing ISC have the urethral catheter removed 14 days post-operatively––this is to avoid inadvertent damage to the vaginal wound, particularly as many of these patients have little or no sensation in this area.

Our primary outcome measurement was objective success of the procedure (measured with pad use). Secondary outcomes were International consultation on incontinence questionnaire – urinary incontinence (ICIQ-UI) scores and complication rates according to Clavien–Dindo classification [6]. The median and interquartile range was calculated as it is less screwed by extreme values in smaller sample sizes.

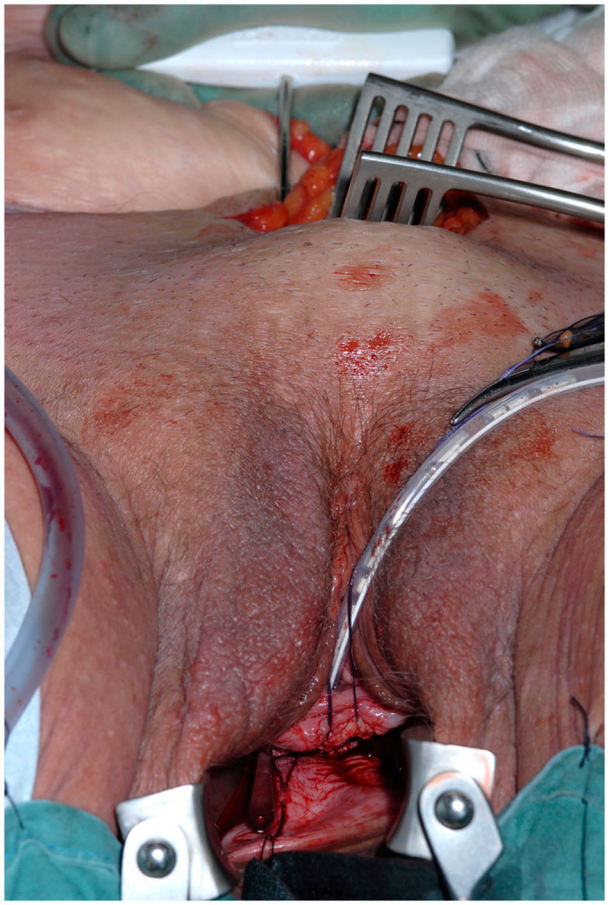

Fig. 1 Curved McGuire needle. Parkes anal retractor used to access vagina. Maguire needle passed retropubically to dissected paraurethral area.

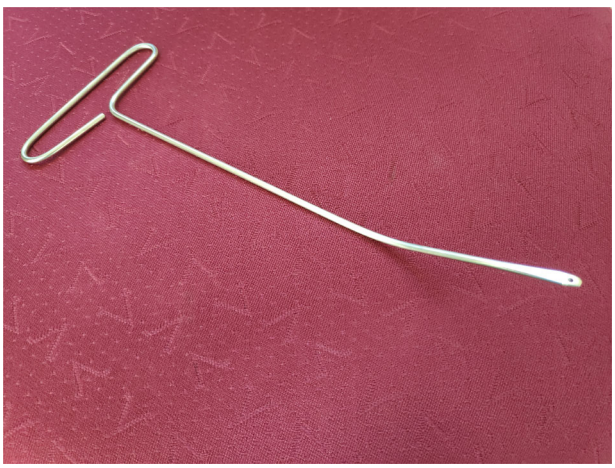

Fig. 2 Adapted McGuire needle.

RESULTS

Three patients had sacral pressure sores which were slow to heal in part due to severe incontinence. Surgical management of their pressure sores was postponed until they had undergone treatment of their incontinence.

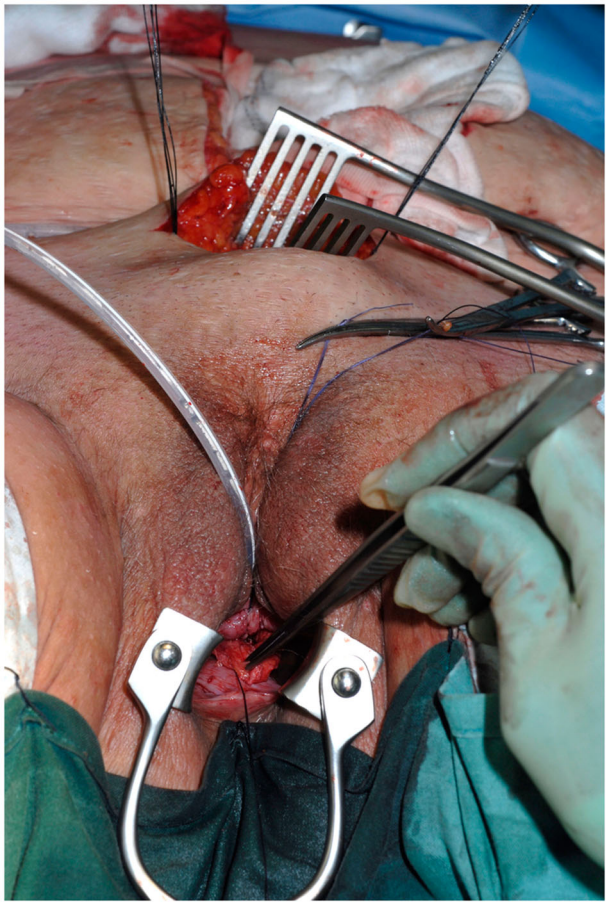

Fig. 3 Two ends of the suture seen to be pulled through the suprapubic incision to be tied over the rectus fascia.

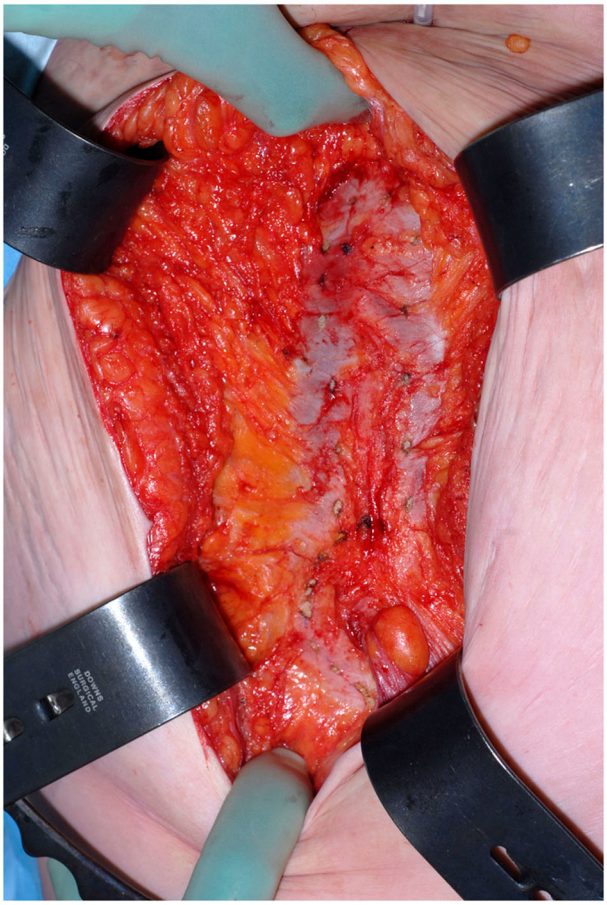

Fig. 4 Rectus fascia ready for harvest as sling. Note; this picture is taken from a laparotomy incision.

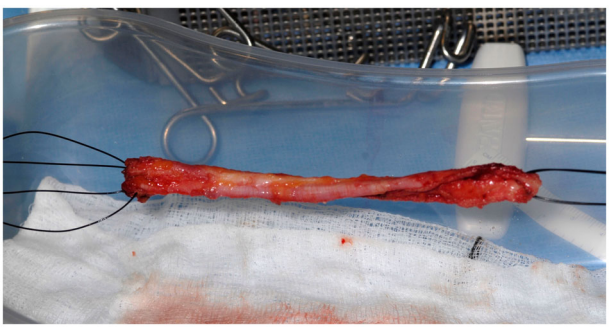

Fig. 5 Rectus fascia strip loaded on sutures to create a 'sling on a string'.

The median bladder capacity was 500 ml (interquartile range 325 ml–574 ml). Three patients had evidence of NDO on urodynamics despite being on anticholinergic medications and therefore two patients proceeded to intradetrusor botulinum toxin A administration at the time of sling insertion after counselling. Only one patient demonstrated poor compliance at the end of filling (500 ml) however she was safely managing her bladder with ISC at lower volumes.

The median length of stay was three days (quartiles 2–5.5 days) with no unplanned readmissions and there was no mortality. Eight patients had an additional planned procedure during sling insertion (two botulinum toxin A injections, one cystolithopaxy, one insertion of SPC, two vaginal hysterectomy, one patient had an Achilles tendon lengthening procedure and one anterior vaginal repair–carried out by an experienced urogynaecologist). Median length of follow-up was 21.5 months (quartiles 6.5 months–31.25 months).

The typical pad use decreased from five pads per day pre-operatively to 0.28 post-operatively while the mean ICIQ-UI score decreased from 17.2 to 1. Nineteen patients were completely dry i.e. no pad use (86.4%) and two had improvement (9.1%). One patient unfortunately developed recurrent SUI at 28 months post-procedure (4.5%), having initially been completely continent.

As expected, patients who pre-operatively required ISC or SPC continued on this management post-operatively (17 patients). Three patients required de-novo ISC post-procedure however they had been counselled regarding the high risk of retention and had been successfully taught to perform ISC pre-operatively. Two patients were able to void spontaneously while maintaining urinary continence. One patient developed de novo detrusor overactivity which was successfully managed with anticholinergic medication.

There were three Clavien–Dindo grade III–IV post-operative complications (13.6%). One patient developed a severe lower respiratory tract infection which required high dependency unit (HDU) admission for antibiotics and inotropic support. Two patients developed wound problems. The first was a lady with tetraplegia who had also been treated for a large perineal pressure sore extending into her pelvis who developed a wound infection and haematoma associated with the pressure sore which needed drainage in theatre. The second developed a wound infection which needed a vacuum-assisted closure (VAC) dressing to heal. Both patients recovered completely and were dry. Of these three patients who suffered Clavien–Dindo III–IV complications, two had

Table 1. Patient Demographics and baseline characteristics.

Patient	Age	Neurological diagnosis	Mobility	Pre-op catheter use	Pre-Op NDO treatment
1	41	Disc Surgery L4/5	wheelchair	SPC	No
2	80	T12 AIS A SCI	wheelchair	SPC	Yes
3	75	T6 AIS A SCI	wheelchair	SPC	Yes
4	34	Disc Surgery L5	ambulant	SPC	Yes
5	65	Multiple Sclerosis	wheelchair	SPC	Yes
6	34	Transverse Myelitis (T12 level)	wheelchair	SPC	Yes
7	52	T8 AIS A SCI	wheelchair	SPC	No
8	51	T12 Disc Surgery	wheelchair	SPC	Yes
9	45	Congenital anorectal abnormality	ambulant	ISC	Yes
10	53	Cauda Equina Syndrome	ambulant	ISC	Yes
11	59	T10 AV malformation	wheelchair	ISC	No
12	43	L4/5 Disc Surgery	crutches	ISC	Yes
13	35	Myeloencephalitis	ambulant	ISC	Yes
14	49	L3/4 Disc Surgery	wheelchair	ISC	No
15	72	L2 AIS A SCI	ambulant	ISC	Yes
16	49	Transverse Myelitis (T9 level)	ambulant	ISC	Yes
17	19	Cauda Equina Syndrome	ambulant	ISC	No
18	56	Multiple Sclerosis	ambulant	None	Yes
19	53	L4/5 Disc Surgery	crutches	None	No
20	45	L5/S1 SCI	ambulant	None	Yes
21	54	L5/S1 SCI	ambulant	None	Yes
22	26	Intracranial Hypertension	ambulant	None	Yes

SCI spinal cord injury, *SPC* suprapubic catheter, *ISC* intermittent self-catheterisation, *AV* arteriovenous, *AIS* American Spinal Injury Impairment Scale, *NDO* neurogenic detrusor overactivity.

planned concurrent procedures (vaginal hysterectomy and botox injections).

The three patients with sacral pressure sores had an uncomplicated recovery following surgery. Two continued with non-surgical management and subsequent healing of their pressure sores which had been impaired by the SUI. One patient underwent surgical debridement and wound management which had been delayed until her sling surgery; her pressure ulcer subsequently healed well.

DISCUSSION

Stress urinary incontinence in the neurogenic population is a significant disabling feature of urinary tract dysfunction. There are multiple different management options for neurogenic stress urinary incontinence including bulking agents, mid-urethral synthetic tapes, autologous pubovaginal fascial slings, colposuspension, insertion of an artificial sphincter and in extreme cases urethral closure. Another consideration in the neurogenic cohort is the presence of co-existing NDO. Patients with both NDO and SUI may benefit from an augmentation cystoplasty performed at the same time as any SUI procedure and should be fully investigated and counselled regarding this option. In our patient cohort the majority of patients were already on treatment for NDO pre-operatively (either pharmacological or botulinum toxin injections) and two patients had intradetrusor botulinum toxin injections intraoperatively. All these patients were counselled fully regarding the more permanent option of augmentation cystoplasty, but they were either deemed as unsuitable (e.g. unable to do ISC/bladder washouts or underlying renal/liver dysfunction) or declined the procedure.

Patients in this cohort had different neurological aetiologies. Those with low spinal injuries, transvers myelitis and cauda equina were likely to have lack of sphincter innervation secondary to the injury, this includes the patient with anorectal malformation who had a low vertebra deficiency. Our patient with multiple sclerosis was clinically like a tetraplegic patient and had had a urethral catheter in situ for a long time which was probably the main cause of their SUI. Those patients with suprapontine injuries have a less clear-cut mechanism for their stress incontinence however they also had a history of long-term urethral catheterisation.

Bulking agents have been found to have poor long-term outcomes and at the present time are only utilised in our unit in patients unfit for other procedures [2]. The use of synthetic tapes has not been advised in the UK for patients with nSUI due to the risk of urethral tape erosion however, there have been some studies showing varying degrees of success. Hamid et al. reported outcomes from a retrospective evaluation of the tension-free vaginal tape (TVT) in 12 women with spinal cord injuries; reporting dry rates of 83.3% and improvement in a further 8.3% at a mean follow-up of 27.1 months [7]. El-azab et al. demonstrated comparable treatment outcomes between TVT and PVS, in a non-randomised clinical trial, evaluating women with SUI and with pathology below S2, i.e., lower motor neurone lesions [8]. However, Pannek et al. performed a retrospective review of 9 women with a spinal cord injury who underwent a sub-urethral transobturator tape for urodynamic proven nSUI, reporting a success rate of 33% and concluded that TOT insertion in this group of patients resulted in unfavourable results [9]. Currently in the UK there is a pause on the insertion of synthetic tapes due to complications such as dyspareunia, tape erosion and chronic pain and therefore alternatives are all the more important.

Insertion of an artificial urinary sphincter remains a management option for nSUI however, there is a lack of evidence in the literature for its use in female patients. Patki et al. reported success rates of 77% in the male nSUI population however associated with a high revision/explanation rate (65.4%) [10]. Compared to AUS

insertion in non- neurogenic patients, women with NLUTD appear to have higher rates of device failure and reoperation as well as a raised potential for infection and erosion [11]. This message was echoed in one systematic review examining the surgical treatment of nSUI, albeit without the inclusion of RCTs, and revealed an overall success rate of 64% with median follow-up of 48 months [12]. Although good outcomes have been reported the high revision rate, limited lifespan of the device and potential for infection and erosion make the AUS less likely to be used as first line treatment for stress incontinence in women.

The evidence to support the insertion of PVS in the non-neurogenic population is well documented. Success rates in the non-neurogenic female population range from 67–93%, with the SISTEr trial showing that PVS was superior to Burch colposuspension at 2-year follow-up (66% cure vs 49%) [4]. The evidence for PVS is also well established in the paediatric neurogenic population (94.44% continence rates) [13] and males with neurogenic urethral incompetence (83% success rates) [14] however, the evidence for its use in the adult female neurogenic population is very limited. Indeed, Teplitsky et al. found a paucity of good quality evidence for the management of urinary tract dysfunction in women with spinal cord injuries and identified large gaps in knowledge with a relatively small evidence bases to support treatment options [15]. To our knowledge Athanasopoulos et al. have reported outcomes from the largest cohort of neurogenic women undergoing PVS insertion. They performed a retrospective review of 33 patients who underwent PVS for neurogenic stress urinary incontinence (21 spina bifida and 12 spinal cord injuries). 75.75% of patients were dry following the procedure with a further 15.15% improved. In addition, Fontaine et al. reported outcomes of 21 patients who had undergone both PVS insertion and augmentation ileocystoplasty with a completely continent rate of 95.2% [16]. Our outcomes are comparable to the literature, with 86.4% of patients dry and 9.1% improved however neither of these studies used the ICIQ-UI scores therefore these cannot be compared. It should also be noted that our median duration of follow-up (21.5 months), is relatively short, perhaps contributing to the favourable dry rate, but direct comparisons between these studies are difficult to make.

The two most important complications described following PVS insertion are de novo urgency and urinary retention and are relatively higher in these patients than those that undergo Burch colposuspension and indeed insertion of synthetic tapes. De novo urgency has been reported in 15–20% and urinary retention 5–20% [17]. However, the neurogenic population are somewhat different to the non-neurogenic as the vast majority manage their bladders with catheterisation (either intermittent self-catheterisation or long-term suprapubic catheterisation). In our practice all patients are fully counselled regarding the higher risk of urinary retention and all are either taught to self-catheterise or expect to have an indwelling catheter post-operatively.

In Athanasopoulos et al.'s cohort, five patients had complications following the procedure (15.2%); with de novo overactivity reported in 6% of patients (two patients) and three patients requiring surgical treatment for a sling erosion, urethral stenosis and vesico-vaginal fistula [18]. Whilst we had a slightly lower complication rate, our rate of de novo overactivity was similar at 4.5%. Only one patient had recurrent SUI at 28 months following insertion of a PVS. This lady had a long history of a T6 AIS A spinal cord injury with significant disability as well as an increased BMI and difficulties managing sacral pressure sores. In addition, she had a somewhat patulous urethra on initial presentation that may have unfortunately put her at increased risk of developing recurrent SUI. It is important to fully assess the quality of urethral and vaginal tissue in neuropathic patients in order to counsel them regarding the future risk of recurrent SUI.

Surgery of any description carries an inherent risk of wound infection; a complication unfortunately experienced by two of our patients, one of whom required a VAC dressing to assist with healing. The risk of abdominal wound infection may be greater in patients with neurogenic lower urinary tract dysfunction who mobilise with a wheelchair, particularly those who have a larger body habitus where the wound may lie in a skin fold prone to moisture. It is important to minimise the risk of infection by following local antibiotic prophylaxis guidelines and national guidelines to prevent surgical site infection [19].

CONCLUSION

Stress urinary incontinence in the female neurogenic population has a profound impact on the quality of life of affected individuals, particularly those with pressure ulcers. There remains a paucity of evidence in the literature to support the treatment options in this cohort of patients. This study supports the use of the autologous pubovaginal sling in patients with neurogenic stress incontinence, with a continent rate of 86.4% at last follow-up and an acceptable morbidity rate. Larger prospective studies using both validated objective outcome measures and patient reported outcome measures would be a welcome addition to the literature to inform management guidelines for neurogenic stress incontinence in the female population.

DATA AVAILABILITY

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Luber KM. The definition, prevalence, and risk factors for stress urinary incontinence. Rev Urol. 2004;6:3.
2. Taweel W Al, Seyam R. Neurogenic bladder in spinal cord injury patients. Research and Reports in Urology. 2015;7:85–99.
3. McGuire EJ, Lytton B. Pubovaginal sling procedure for stress incontinence. J Urol. 1978;119:82–4.
4. Albo ME, Richter HE, Brubaker L, Norton P, Kraus SR, Zimmern PE, et al. Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. N Engl J Med. 2007;356.
5. National Institute for Health and Care Excellence. Urinary incontinence in neurological disease: assessment and management | Guidance | NICE. NICE Guidelines. 2012.
6. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications. Ann Surg. 2004;240:205–13.
7. Hamid R, Khastgir J, Arya M, Patel HRH, Shah PJR. Experience of tension-free vaginal tape for the treatment of stress incontinence in females with neuropathic bladders. Spinal Cord. 2003;41:118–21.
8. El-Azab AS, El-Nashar SA. Midurethral slings versus the standard pubovaginal slings for women with neurogenic stress urinary incontinence. Int Urogynecol J. 2015;26:427–32.
9. Pannek J, Bartel P, Gocking K. Clinical usefulness of the transobturator suburethral tape in the treatment of stress urinary incontinence in female patients with spinal cord lesion. J Spinal Cord Med. 2012;35:102–6.
10. Patki P, Hamid R, Shah PJR, Craggs M. Long-term efficacy of AMS 800 artificial urinary sphincter in male patients with urodynamic stress incontinence due to spinal cord lesion. Spinal Cord. 2006;44:297–300.
11. Murphy SM, Rea D, O'Mahony J, McDermott TED, Thornhill J, Butler M, et al. A comparison of the functional durability of the AMS 800 artificial urinary sphincter between cases with and without an underlying neurogenic aetiology. Ir J Med Sci. 2003;172:136–8.
12. Farag F, Koens M, Sievert KD, De Ridder D, Feitz W, Heesakkers J, et al. Surgical treatment of neurogenic stress urinary incontinence: A systematic review of quality assessment and surgical outcomes. Vol. 35, Neurourology and Urodynamics. 2016;21–5.
13. Austin PF, Westney OL, Leng WW, McGuire EJ, Ritchey ML. Advantages of rectus fascial slings for urinary incontinence in children with neuropathic bladders. In: J Urol. 2001;2369–71.
14. Daneshmand S, Ginsberg DA, Bennet JK, Foote J, Killorin W, Rozas KP, et al. Puboprostatic sling repair for treatment of urethral incompetence in adult neurogenic incontinence. J Urol. 2003;169:199–202.

15. Teplitsky S, Murphy A, Shenot PJ. Knowledge Gaps in Urologic Care of Female Spinal Cord Injury Patients. Vol. 20, Current Urology Reports. 2019.
16. Fontaine E, Bendaya S, Desert JF, Fakacs C, Le Mouel MA, Beurton D, et al. Combined modified rectus fascial sling and augmentation ileocystoplasty for neurogenic incontinence in women. J Urol. 1997;157:109–12.
17. Athanasopoulos A, Gyftopoulos K, McGuire EJ. Efficacy and preoperative prognostic factors of autologous fascia rectus sling for treatment of female stress urinary incontinence. Urology. 2011;78:1034–8.
18. Athanasopoulos A, Gyftopoulos K, McGuire EJ. Treating stress urinary incontinence in female patients with neuropathic bladder: The value of the autologous fascia rectus sling. Int Urol Nephrol. 2012;44:1363–7.
19. National Institute for Health and Care Excellence. Surgical site infections: prevention and treatment NICE guideline (NG125). https://www.nice.org.uk/guidance/ng125. 2019;(April).

AUTHOR CONTRIBUTIONS

All authors have contributed to the design and development of this manuscript. More specific author contributions are listed as follows: AD: Conception of manuscript, analysis and interpretation of data. Revising critically for important intellectual content. Final approval of the work to be published. Agreement to be accountable for all aspects of the work. AD: Conception of manuscript. Interpretation of data. Involved in revision of manuscript and final approval of work to be published. AM: Conception of manuscript. Data interpretation and critical revision. SR: Conception of manuscript. Critical revision. Agreement to be accountable for all aspects of the work.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to A. Deytrikh.