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Original Article

Reinnervation of the neurogenic bladder in the late period of the spinal cord trauma

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Study design: Intercostal nerve to spinal nerve root anastomosis in chronic spine-injured patients.
Objectives: To analyze the effectiveness of neurogenic bladder reinnervation in spinal cord-injured patients through artificial creation of sprouting (intercostal nerve to spinal nerve root anastomosis).
Setting: Center of Neurosurgery, Moscow, Russia. Operations were performed by Professor A Livshits. (At present, Professor A Livshits is working at the Spinal Care Unit, Meir General Hospital, Kfar Saba, Israel.)
Methods: A total of 11 patients with spinal cord injury of the L1 level were operated on in the late (chronic) stage. The neurological status and urodynamics were investigated before and 12 months after operation. A laminectomy from T11 to L3 was performed. Next, a neurolysis of the 11th and 12th intercostal nerves was carried out, at a distance of 20–21 cm, and transferred to the vertebral canal. The S2–S3 roots were then cut in their proximal portion and anastomosed end-to-end to the intercostal nerves. The results of urodynamic studies were calculated by the Wilcoxon signed rank test for comparison before and 12 months after operation.
Results of urodynamic studies: Bladder capacity (ml) before operation – 489 ± 79, after operation – 350 ± 39, urine volume (ml) before – 18.2 ± 17, after – 306.4 ± 39.8, residual urine (ml) before – 459 ± 99.4, after – 50 ± 11.8. Detrusor tone (rel. units) before – 0.6 ± 1.5, after 1.2 ± 0.2; voiding pressure (cmH_2O) before – 4.4 ± 5.2, after – 30.5 ± 4.9. Force of detrusor contraction before – 5 ± 5.8, after – 32.8 ± 5.5. Sphincter resistance (cmH_2O) before – 6.5 ± 3.8, after – 21.1 ± 4.2. Significant improvements in bladder function were observed during the 10th to 12th postoperative months. Restoration of reflex voiding occurred in all patients; in eight of the 11 paresthesic in the groin and scrotum and reappearance of the bulbocavernous, anal and cremasteric reflexes were noted.
Conclusion: These results suggest that a restitutive process occurs in the bladder under novel conditions of its nerve supply provided by the intercostal nerve and by new connections established between it and the bladder nerves. Spinal cord lesions that might benefit from nerve crossover surgery would be located at the conus, so functional intercostal nerves could be connected to sacral roots to bypass the injury in an attempt to restore central connections to the bladder.
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Keywords: neurogenic bladder; intercostal nerve; reinnervation; urodynamic

Introduction

The realization that accessory pathways of spinal cord innervation could arise through collateral sprouting to bring about restoration of spinal cord function led investigators to look for ways such pathways can be established artificially.

Nerve crossover surgery to bypass a spinal cord injury and reinnervate the neurogenic bladder was first conceptualized in 1907.[1] Both theoretical dissertations and cadaver studies have furthered this concept.[2–4] The reconstruction of spinal roots by anastomosing them to intercostal nerves following spinal trauma with spinal

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cord involvement was described.[2] Several authors[5,6] have pointed out that an intercostal nerve can be used to restore rectal as well as bladder function in spinal cord-injured patients. Nerve crossover techniques for urinary bladder reinnervation on animals and human cadavers were investigated.[7] If central pathways could be restored to the decentralized bladder through a microneural reconstructive technique, a return of useful function might be achieved.

This anatomical study describes the nerve crossover techniques used in human cadaver dissections for connecting intercostal nerves to sacral roots intraspinally. The techniques were modified from and compared to similar procedures used in an animal model where adjacent extradural roots were connected through a nerve graft. It was shown previously that the unilaterally decentralized bladder of the cat can be recentralized after a nerve crossover procedure. If additional laboratory studies can document the return of useful bladder function, it was anticipated that selected patients may benefit from similar nerve crossover techniques to bypass a spinal cord lesion to recentralize the bladder.

Limited studies on nerve crossover procedures have also been investigated in human patients.[8,9] Although these techniques in several spinal cord-injured and spina bifida patients have realized only minimal success, the results of experimental studies in cats have been more encouraging.[10] The ability of a mixed suprasacral root to recentralize the unilaterally decentralized bladder when connected to a sacral root through a nerve graft allowed the concept of urinary bladder reinnervation to be viewed with cautious optimism.[11–13] If crossover nerve surgery could restore central bladder control and useful bladder function, these patients would gain independence from present methods of bladder emptying, be free from associated medical complications and enjoy an improvement in quality of life.

Experience with bladder reinnervation in spinal cord-injured patients through artificial creation of sprouting has also been achieved in our clinic.

Methods

A retrospective study was undertaken of 11 operations – neurogenic bladder reinnervation by anastomosing S2–S3 roots to 11–12th intercostal nerves – performed on the 11 patients with spinal cord injury. Patients were operated on by Professor A Livshits in the Center of Spinal Neurosurgery, Moscow, Russia. Informed consent from the patients was obtained. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. The patients had complete spinal cord injuries on the L1 level, and dysfunction of pelvic organs. The average follow-up period was 12 months. The mean age of the patients was 30 years with a range from 18 to 47 years. All patients were male. The average duration of pathology was 2 years (a range from 1 to 4 years).

Both spontaneous voiding and the sense of bladder fullness were absent; bulbocavernous, cremasteric and anal reflexes were not elicitable, and cystometrography revealed an areflexic or hyporeflexic bladder. Clinical features are illustrated in Table 1. All patients were investigated regarding urodynamics, EMG of external urethral sphincter, diary of micturition, tests of quality of life and Valsalva test.

Operative procedure

Under endotracheal anesthesia, a standard laminectomy from T11 to L3 was performed with the patient lying prone. (If laminectomy had been performed previously, meningomyeloradiculolysis was carried out in the laminectomy area.)

Next, an incision was made over the 11th and 12th ribs and, after securing hemostasis, neurolysis of these intercostal nerves was effected at a distance of T11–21 cm and T12–20 cm from the costal angle – where these nerves divide into two small-diameter branches. After cutting the nerves at the site of branching, they were transferred to the vertebral canal through a tunnel previously made under deep spinal muscles. The chest wound was completely closed in layers and the intravertebral part of the operation was then continued (Figure 1 (1)).

Under the operative microscope, the cauda equina roots were inspected and separated from adhesions with the arachnoid and from each other. Intraoperative testing of the roots was then started to identify the S2 and S3 roots. The distance between adjacent nerve roots as they leave the spinal cord is in the order of 2.5 cm. An examination of the L5 root showed it to be larger than S1 and in contrast to S1. L5 enters its intervertebral foramen almost at a right angle. S1 has a more oblique course towards its intervertebral foramen. There is also an increase in the size of the thoracic intraspinal extradural roots to S3, and then a decrease in the size for the remaining sacral and coccygeal roots. The intraspinal course of the extradural roots is about the same until the S2/S3 level is reached, after which their course lengthens slightly. The S2 and S3 dorsal root ganglia lie intraspinally, while for the more rostral roots they lie adjacent to or within the intervertebral foramen.

The S2 intradural roots enter the cord at the lower level of the L1 vertebra. For each sacral nerve root, the combined diameter of the dorsal and ventral intradural root component was at least 50% greater than that of an intercostal nerve in its mid-part. The dorsal root component was consistently larger than the ventral root component.

Furthermore, the dorsal and ventral root components were still visible immediately distal to the dorsal root ganglion, and therefore could be matched reasonably well in a crossover anastomosis. Such matching may improve alignment of regenerating motor and sensory axons to appropriate endoneurial tubes, which may facilitate reinnervation especially when the dominant root to the bladder is chosen.[7] The S2 and S3 roots are

Table 1 Clinical features

NN pts	Age (years)	Sex	Years after trauma	Level of trauma	Level of PPL	Level of anasthesia	Bladder capacity (ml)		Urine volume (ml)		Residual urine volume (ml)		Defrusor tone (rel.units)		Voiding pressure (cmH_2O)		Force of defrusor condition (cmH_2O)		Spincter resistance (cmH_2O)		Bulbocavern reflex		Cremasteric reflex		Anal reflex	
							B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A
1	19	M	2	L_1	L_1	L_1	1150	350	0	280	1150	60	0.5	1.2	0	75	0	35	10	15	0	+	0	+	0	+
2	24	M	1.7	L_1	L_1	L_1	475	350	0	240	470	70	0.7	1.0	0	27	0	30	7	17	0	+	0	+	0	+
3	18	M	1.5	L_1	L_1	L_1	495	340	25	280	470	40	0.8	1.4	5	30	5	30	3	22	0	+	0	+	0	+
4	47	M	3	L_1	L_1	L_1	600	420	40	370	550	50	0.4	0.9	7	37	8	40	5	25	0	0	0	0	0	0
5	30	M	1	L_1	L_1	L_1	440	350	20	290	400	60	0.8	1.3	4	29	7	29	3	20	0	+	0	+	0	+
6	27	M	4	L_1	L_1	L_1	385	300	25	350	260	40	0.8	1.5	5	32	5	35	4	24	0	+	0	+	0	+
7	42	M	2.5	L_1	L_1	L_1	410	350	20	300	390	50	0.6	1.2	4	28	4	27	3	20	0	0	0	0	0	0
8	34	M	1.5	L_1	L_1	L_1	450	310	50	280	400	30	0.7	1.2	18	42	20	45	12	30	0	+	0	+	0	+
9	40	M	1.2	L_1	L_1	L_1	500	400	20	360	480	40	0.5	1.1	5	30	6	32	3	22	0	0	0	0	0	0
10	29	M	2.3	L_1	L_1	L_1	650	380	0	320	650	60	0.4	0.8	0	27	0	30	10	19	0	+	0	+	0	+
11	32	M	1.8	L_1	L_1	L_1	480	250	0	300	480	150	0.6	1.2	0	28	0	28	12	18	0	+	0	+	0	+

PPL, paraplegia; B, before operation; A, after operation

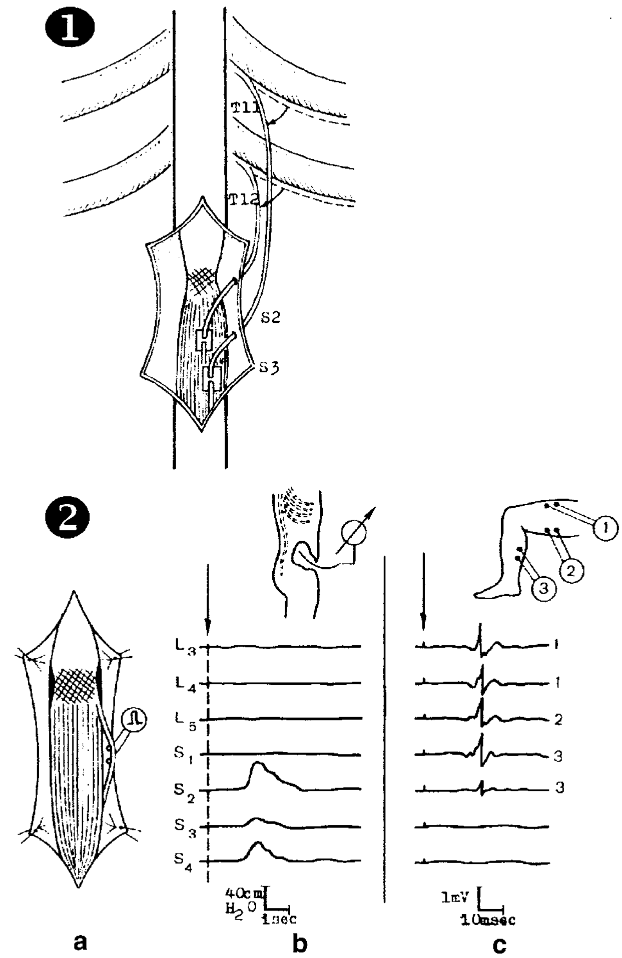

Figure 1 (1) Establishment of microsurgical anastomoses between T11–T12 and S2–S3 roots. (2) Intraoperative testing of spinal roots by electrostimulation. (**a**) Schematic; (**b**) cystometrogram; (**c**) muscle action potentials: 1–m. quadriceps; 2–m. biceps femoris; 3–m. triceps surae

identified by their reaction to electrostimulation as reflected in the intravesicular pressure elevation during the stimulation (Figure 1(1 + 2)).

The S2 and S3 roots were then cut in their proximal portion and anastomosed end-to-end to the intercostal nerves. The anastomosis was accomplished by sewing together two or three fascicles with endofascicular silk (10-0) suture after placing one or two guiding perineurial sutures. During the operation, a square (2 × 2 cm) piece of polymeric film was placed under the intercostal and spinal nerve ends, taking care to ensure that these ends lie freely without tension in the middle of the film. A guiding and reinforcing perineurial suture was placed additionally. After having removed blood and moisture from the film with an aspirator and swabs, one or two drops of the biologic glue was applied to the inner surfaces of both film edges, and the film was wrapped around the nerve ends in such a way that one edge lay on the nerves and the other on the film itself. After 1 or 2 min (when the adhesive had hardened), the residual

Table 2 Results of urodynamic studies before and 12 months after operation

Parameters of bladder function	*Before operation*	*After operation*	*P-Value**
Bladder capacity (ml)	489±79	350±39	0.003
Urine volume (ml)	18.2±17	306.4±39.8	0.003
Residial urine volume (ml)	459±99.4	50±11.8	0.003
Defrusor tone (rel. units)	0.6±0.15	1.2±0.2	0.003
Voiding presure (cmH_2O)	4.4±5.2	30.5±4.9	0.003
Force of defrusor condition(cmH_2O)	5±5.8	32.8±5.5	0.003
Sphincter resistance (cmH_2O)	6.5±3.8	21.1±4.2	0.003

**P*-values were calculated by the Wilcoxon signed rank test for comparison before operation and 12 months after operation

blood was aspirated from the operative area and the dura and wound were completely closed.

Results

After analyzing patients' urodynamics before and after operations, we found that significant improvements in bladder function were observed during the 10th to 12th postoperative months. Bladder capacity (ml) was as follows: before operation – 489±79, after operation – 350±39; urine volume (ml) before – 18.2±17, after – 306.4±39.8; residual urine (ml) before – 459±99.4, after – 50±11.8; detrusor tone (rel. units) before – 0.6±0.15, after – 1.2±0.2; voiding pressure (cmH_2O) before – 4.4±5.2, after 30.5±4.9; force of detrusor contraction before – 5±5.8, after – 32.8±5.5; sphincter resistance (cmH_2O) before – 6.5±3.8, after – 21.1±4.2 (Table 2). Restoration of reflex voiding occurred in all patients; in eight of the 11 patients paresthesia in the groin and scrotum and reappearance of the bulbocavernous cremasteric and anal reflexes were noted. The improvements in micturitional function correlated with those in urodynamic parameters (Figures 2(1+2), 3(1+2) and 4). Three patients had incomplete reflex of voiding and Valsalva maneuver used for micturition (Figure 5(1+2)).

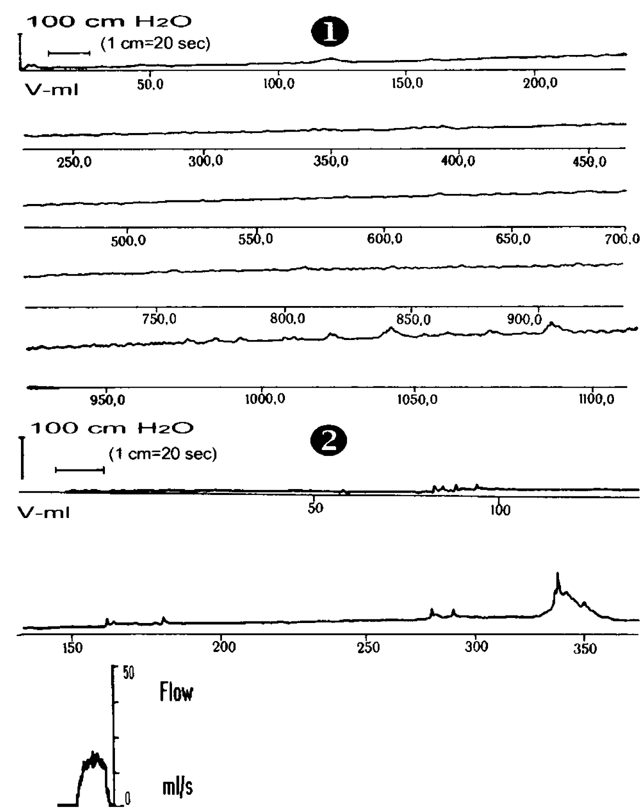

Figure 2 Urodynamics of patient K: before (1), bladder volume more than 1100 cm^3, no leakage occurred, areflexia and 12 months after operation (2), bladder volume 350 cm^3, reflex of micturition, and leakage occurred, leak point pressure 165 cmH_2O, 60 cm^3 residual urine

Discussion

In fact, attempts to create additional collateral innervation for the spinal cord by neurosurgical means date back to the beginning of this century. The first sacral or seventh lumbar nerve were sutured to the second or third sacral nerve, which was said to have resulted in the recovery of bladder and rectal functions.[14] In experiments on dogs, roots of the seventh lumbar nerve were connected to the second and third ipsilateral sacral nerves after 9–11 months, and an identical operation was carried out on the other side, and 9–11 months later the spinal cord between the L7 and S2 segments was transected. Good results were recorded in two dogs.[14]

Experiments on cats indicated that functional recovery of a transected posterior root could occur if the transection site was distal to the respective ganglion.[15,16] This finding encouraged the authors to attempt reinnervation of the urinary bladder. In cats they divided the S1 and S2 roots, which innervate the bladder, and anastomosed the cut ends to the rostrally located spinal roots divided below their ganglia. After 8–10 months, most of the animals showed recovery of bladder function, and this was confirmed by electrophysiological studies.

In our previous experiments[17] where an intercostal nerve was connected to the S2 root by means of a biologic glue, we observed a breakdown of axons and myelin fibers at the proximal end of the posterior S2 root during the first 3 weeks after its sectioning, followed by remyelinization with the appearance of growth cones in nerve fibers toward the end of the third month.

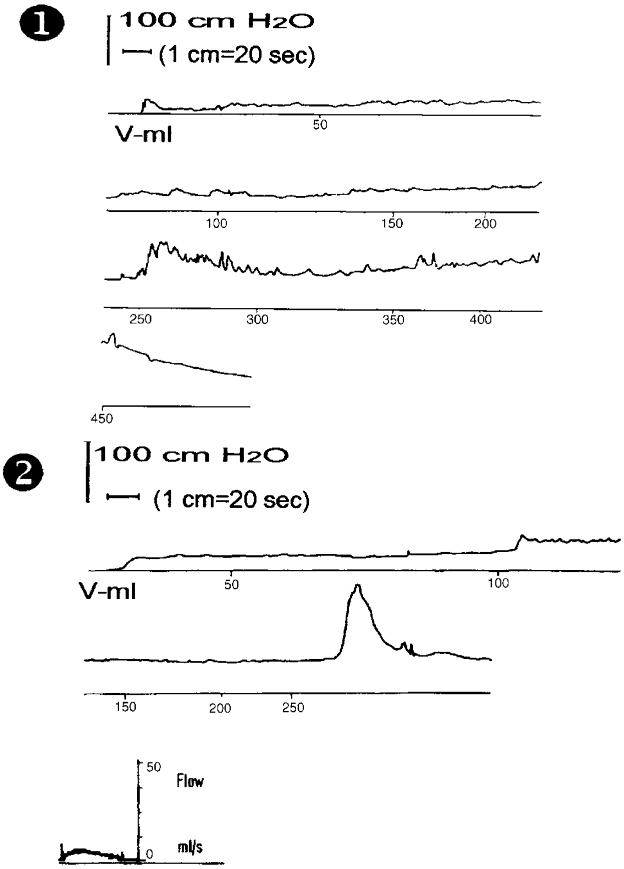

Figure 3 Urodynamics of patient D: before (1), bladder volume 480 cm^3, no leakage occurred and 12 months after operation (2), urodynamics showed loss of urine only during increases in abdominal pressure with an abdominal leak point pressure 200 cmH_2O, 50 cm^3 residual urine

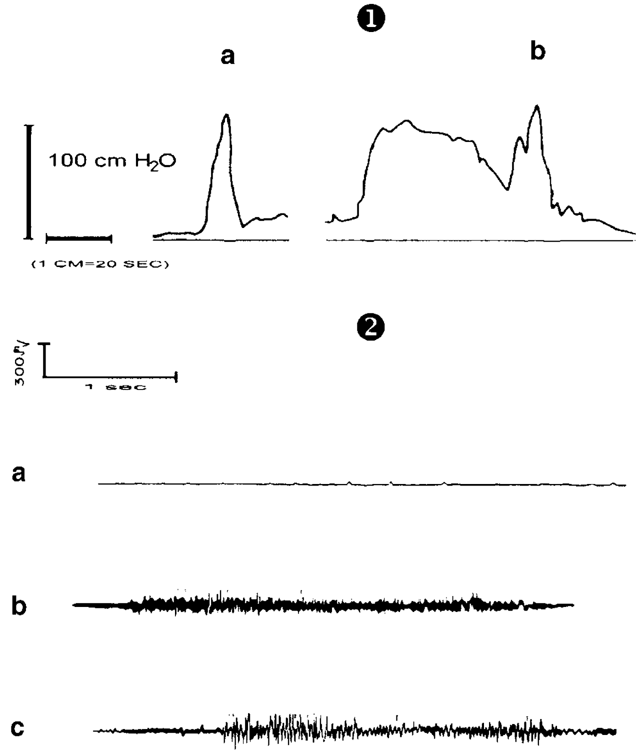

Figure 5 Valsalva maneuver (1) and EMG of external urethral sphincter (2): **a** – before operation; **b** – 6 months and **c** – 12 months after operation. Cystometrogram shows performance of the Valsalva leak point test. Baseline bladder pressure is 12 cmH_2O. On Valsalva to 100 cmH_2O, leakage occurred. Valsalva leak point is 88 cmH_2O (100 to 12 cmH_2O). EMG showed an increase of electrical activity of external urethral sphincter after operation

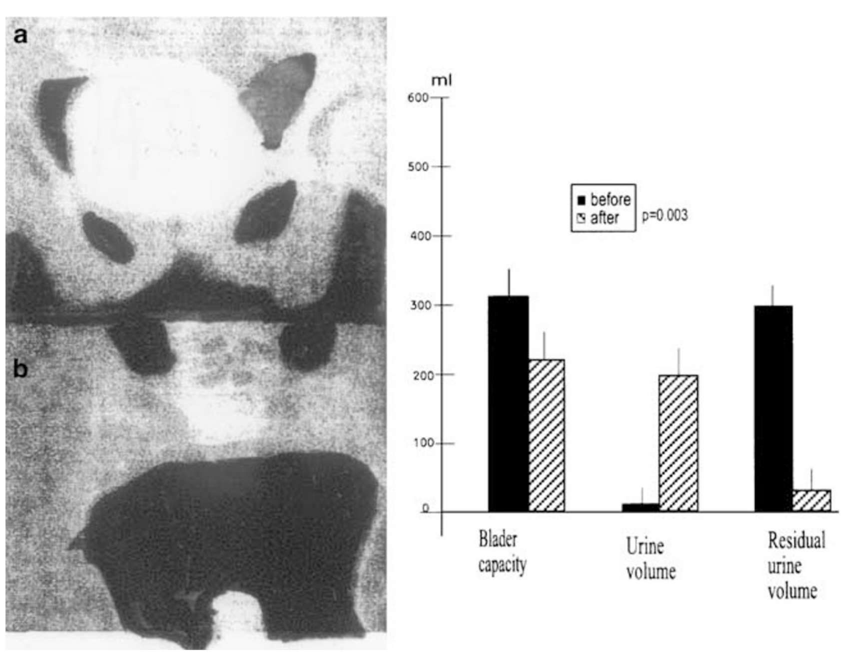

Figure 4 Cystograms of patient K: before (**a**) and 12 months after operation (**b**) – left side, and analysis of bladder functions in our patient – right side

In other studies, the return of bladder contractility has been generally successful.[18,19] Microsurgical repair of nerve roots has been reported previously, but the usefulness of this technique is unclear since the return of the micturition reflex has been documented after simple approximation of nerve ends using a millipore tubulation technique.[20] The time for return of the micturition reflex in these animals who had ventral root only anastomoses varied between 4 and 7 months. The present techniques of nerve anastomosis may be the primary limiting factor in the achievement of useful function. In view of this problem, a new method of reconnecting peripheral nerves resulting in an improved functional return has recently been investigated and may eventually be adapted for nerve root and spinal cord surgery.[21]

One method from the first operation was performed in three patients with gunshot wounds at the T11–L1 level.[14] They connected the T12 root to the S2 root and the L1 root to the S3 root. Satisfactory results were observed in one of the patients, who recovered sensitivity in the gluteal region in 6 months, was able to void spontaneously in 7 months and regained the sense of bladder fullness during the 9th postoperative month. Subsequently, such operations were, however, abandoned probably because strong experimental evidence indicated that functional recovery of the damaged posterior spinal roots was not possible and that the posterior root axons sectioned at the site of their junction with the spinal cord failed to grow into it. Their ingrowth was shown to be prevented by the formation of glial scars.[15]

Subsequently, six patients with paraplegia due to spinal cord trauma were operated.[22] The functional T12 roots above the injury site were transected 2 cm below the posterior ganglion and anastomosed bilaterally to the posterior and anterior S2 and S3 roots mobilized from the injury area. In two cases, restoration of the bladder reflex occurred 8–12 months postoperatively.

The rationale for the use of intercostal nerves as an artificial sprouting is that these nerves are fairly long, contain large numbers (1200–1300) of motor and sensory fibers, and are therefore convenient for surgical establishment of connections with various nerve trunks. For example, the motor and sensory portions of an intercostal nerve were connected, respectively, to the motor and sensory nerve trunks of the brachial plexus.[23,24]

Preliminary studies on a spina bifida patient and several paraplegic patients have indicated that the taking of intercostal nerves above the injury site does not appear to increase the neurologic deficit.[25] Furthermore, in these studies the level of the spinal cord lesion was taken as the indicator of whether a crossover procedure was technically feasible rather than the type of neurogenic bladder dysfunction. The crossover techniques appear to be limited to lesions of the lower thoracolumbar and sacral cord. Spinal cord lesions above this level would require nerve grafts of sufficient length such that their viability might be compromised. In addition to having a spinal cord injury localized to this region, patients being considered for nerve crossover surgery should be young and fit, having recovered from spinal shock with stabilization of the level of injury. Careful management of the urinary bladder while awaiting the result of reinnervation surgery will minimize the effects of chronic inflammation on the detrusor. These chronic changes can lead to detrusor fibrosis and prevent the restoration of useful bladder function despite successful axonal regeneration and bladder recentralization.[26] Urodynamics and clinical studies of our patients before and 12 months after operation showed that reflex of voiding, EMG of external urethral sphincter, diary of micturition and quality of life [27] were increased.

The experimental and clinical studies cited above indicate that nerve supply to the urinary bladder can be reinstated along new pathways that arise when sprouting is induced artificially by operation.

Conclusion

Spinal cord lesions that might benefit from nerve crossover surgery would be located at the conus, so functional intercostal nerves could be connected to sacral roots to bypass the injury in an attempt to restore central connections to the bladder. Therefore, the

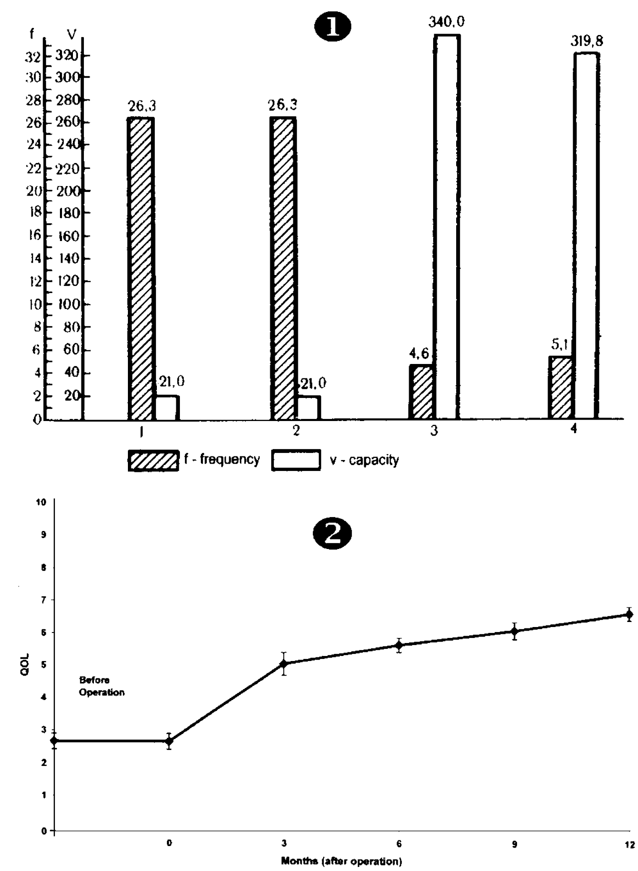

Figure 6 Voiding diary (1) before – left side, 12 months after operation – right side and quality of life (2)

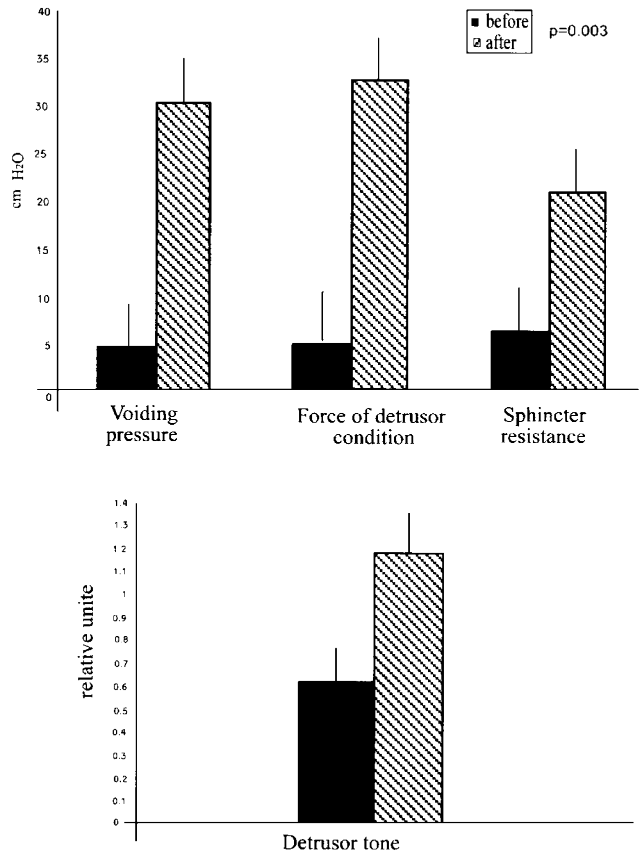

Figure 7 Results of studies of bladder function and urodynamics 12 months after operation

decentralized or neurogenic bladder might be recentralized for restoration of function. The preliminary results (Figures 6 and 7) suggest that regenerative and restitutive processes occur in the bladder under novel conditions of its nerve supply provided by the intercostal nerve and by the new connections established between it and the bladder nerves.

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