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Evaluation of clinical indexes to predict fate of pelvic nerve dysfunction

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Abstract This study was designed to evaluate posterior urethral sensation and sacral reflex evoked by posterior urethral stimulation to predict fate of pelvic nerve dysfunction. Enrolled were 24 male patients sequentially receiving the following examinations 1–3 months (postoperative) and more then 6 months (follow-up) after surgery for rectal cancer: sensory thresholds of the penile skin (SS) and the posterior urethra (SU), sacral reflex evoked by penile stimulation (BCR) and posterior urethral stimulation (UUR), and urodynamic study. Controls included 25 patients with normal voiding function before pelvic surgery. SS, SU and latencies of BCR and UUR averaged 1.9 ± 0.6 mA, 5.6 ± 1.8 mA, 33.3 ± 4.2 ms and 65.0 ± 9.3 ms in controls, respectively, and unchanged postoperatively in 13 patients with normal voiding function. Of 11 patients with voiding dysfunction whose SS and latency of BCR remained unchanged, SU increased in 7, voiding function remained unrecovered in 6 patients during the follow-up period and recovered in the remaining 5. None of four patients with nonevocable UUR recovered voiding function. Thus, unchanged SU and disappearance of UUR were useful to predict recovery and nonrecovery of postoperative voiding dysfunction, respectively.

Key words Sacral reflex · Sensory threshold of the posterior urethra · Pelvic nerve function · Voiding dysfunction

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Introduction

With the spread of extended pelvic lymphadenectomy for intrapelvic organ malignancies with the purpose of controlling local recurrence, the incidence of voiding dysfunction caused by intraoperative injury of the pelvic nerve plexus has markedly increased [12]. Voiding dysfunction not only spoils the quality of life (QOL) of the patient but also threatens life with accompanied urinary infection if urinary management is not adequate. Thus, nerve-sparing surgery has been developed and preserves voiding function much better than extended surgery [9, 17]. Voiding dysfunction, however, has been common shortly after operation; therefore it is interesting clinically to evaluate injury of the pelvic plexus after operation.

Evoked potentials of the sacral reflex have been used to evaluate the sacral reflex arc, which is involved in voiding function [2, 3, 5, 8, 10, 11, 13]. The bulbocavernosus reflex includes contraction of the bulbocavernosus muscle, the anal sphincter, the external urethral sphincter and other perineal muscles elicited by stimulation of the penile or clitoridean skin. By using electrical impulses for stimulation and electromyographic technique for recording the response of these muscles, latency of the bulbocavernosus reflex is measurable objectively and reproducibly, and therefore has been used for neurophysiological evaluation of spinal cord injury [5, 10], compressive spinal disease [2] and impotence [4]. Both afferent and efferent pathways of the bulbocavernosus reflex are considered to be via the pudendal nerve and the bulbocavernosus reflex is used for evaluation of the somatic component of the sacral reflex arc. It has been reported that the bulbocavernosus reflex has no use in evaluation of voiding and erectile function [11, 13], which are controlled mainly by the pelvic nerves. Contraction of the bulbocavernosus muscle, the anal sphincter, the external urethral sphincter and the other perineal muscles was also elicted by simulation of the posterior urethra or the bladder mucosa. Several

terminologies have been proposed for this reflex such as urethro-anal reflex [4], posterior urethral-anal sphincter reflex [8] and vesico-anal reflex [3]. The afferent pathway of this reflex has been thought to pass through the pelvic plexus. If so, this reflex should be applicable in evaluating the autonomic component of the sacral reflex arc and intraoperative injury of the pelvic plexus.

To elucidate the above assumption, sacral reflexes evoked by stimulation of the penile skin and the posterior urethra, and sensory thresholds of the penile skin and the posterior urethra of patients who received surgery for their rectal cancer were sequentially examined in combination with urodynamic studies.

Materials and methods

Patients and surgical procedures

Twenty-four male patients who sequentially underwent urodynamic studies (UDS) 1–3 months (postoperative) and more than 6 months (follow-up) after the surgery of their rectal cancer at our institution from June 1990 to December 1994 were enrolled in the current study as the patient group as possibly having operative injury of the pelvic nerve plexus. Their median age at operation was 54 years with the range from 34 to 76 years. Measures obtained from 25 male patients who presented no voiding dysfunction in UDS before the surgery of their rectal cancer were used as normal controls, including 15 of the patient group described above. Their age ranged from 34 to 76 years with the median of 57 years. All control patients were neurologically normal and none had invasion of the rectal cancer into the urinary tract.

Nerve-sparing operations for rectal cancer were carried out in all patients. The lateral lumbar splanchnic and bilateral hypogastric nerves and the superior hypogastric and pelvic plexuses were identified and selectively preserved [17]. At least the lower half of the unilateral pelvic plexus was preserved, although the amount of nerve-sparing was different in each patient.

Measurement of sensory threshold

The electrostimulus and electromyography were done using Neuromatic 2000 (Dantec Medical, Skovlunde, Denmark). The patient was placed in the lithotomy position. The penile skin was stimulated using two surface plate electrodes, type of 13L20 (Dantec) placed on the dorsum of the penile shaft at 10 mm distance, with the cathode proximal to the anode. A 14-F indwelling balloon catheter with two ring electrodes (2 mm wide) mounted 15 and 25 mm from the base of the balloon (Nihon Kohden Co., Tokyo, Japan) was used for stimulation of the posterior urethra. After the balloon was filled with water, the indwelt catheter was retracted to allow direct contact of electrodes with the mucosa of the posterior urethra. The bladder was kept emptied throughout the procedure. The posterior urethra and the penile skin were stimulated with square wave stimuli of 0.2 ms duration with 1 Hz frequency. The stimulus intensity was slowly increased from 0.1 mA until occurrence of subjective feeling of the stimulus or up to 99.9 mA. This procedure was repeated three times and the lowest value was defined as the sensory threshold.

Detection of action potential of the external sphincter

Electromyographic responses of the external urethral sphincter were recorded using a concentric needle electrode of type 13L49 (surface area 0.07 mm^2, Dantec). The needle electrode was inserted toward the apex of the prostate from the perineal skin 2–3 cm anterior to the anus guided by a finger in the rectum. In the patient after abdominoperineal resection, the needle electrode was inserted in the same position and correct needle placement was confirmed by audio and oscilloscopic monitoring of motor unit action potentials aroused by prodding the electrode in to the external urethral sphincter.

Induction of sacral reflex

In the present study, evoked responses of the external urethral sphincter obtained by the stimulation of the penile skin were designated as the bulbocavernosus reflex and those obtained by the stimulation of the posterior urethra were designated as the urethro-urethral sphincter reflex. Stimulation to evoke sacral reflex was given as strongly as was tolerable, which was usually three to four times stronger than sensory threshold of each patient. The high-pass filters were set at 2 kHz and the low-pass filters at 10 Hz. Sampling times were selected for 100 ms after penile stimulation and for 200 ms after urethral stimulation. The action potential of the external sphincter was recorded as an average line of 50–100 sweeps, with a gain of 10–20 μV/Deviation. The latency of the reflex was measured at the time lag between stimulation and onset of the response on the recorded line. Since it was difficult in some cases to identify the response in a single sweep, we did not measure reflex threshold. Loss of reflex was defined as no response to the stimulation at 60 mA or more.

Urodynamic study (UDS)

UDS was performed in a shield room with UD5500 (Dantec) to confirm presence or absence of voiding dysfunction. After filling by spontaneous diuresis uroflowmetry measured by the rotating disk method in the standing position, residual urine volume was measured by transurethral catheterization. The patient was placed in the lithotomy position and then medium-fill cystometry was performed with CO_2 at room temperature at a constant filling rate of 100 ml/min through a 10-F urethral catheter. Filling was performed until the patient felt full and then he was required to void in the same position. Electromyography of the external urethral sphincter was recorded simultaneously with cystometry [1].

These examinations were carried out in the following order uroflowmetry: residual urine measurement, cystometry, measurement of sensory threshold of the penile skin, the bulbocavernosus reflex, measurement of sensory threshold of the posterior urethra, and the urethro-urethral sphincter.

A normal uroflowmetrogram was defined as an average flow rate more than 10 ml per second without intermittent flow. Residual urine was defined as vesical urine volume more than 30 ml after voiding. Normal cystometrogram during voiding was defined as voluntary detrusor contraction of adequate magnitude and duration during voiding phase [1]. Preoperative voiding function was judged to be normal when the above examinations had normal results; however, two patients had no residual urine and were normal in repeated uroflowmetry but failed to void at cystometry. The discrepancy was presumed to be attributable to psychological disturbance of voluntary voiding by the attendance of other people and position at cystometry. Postoperative voiding dysfunction was judged on the basis of the result of cystometry except for the above two patients whose voiding dysfunction was judged to be normal on the basis of results of urodynamic studies performed preoperatively.

Statistical analysis was made by Fisher's exact test or the Mann-whitney U test.

Results

Postoperative sensory thresholds latencies of sacral reflex, and voiding dysfunction

Representative profiles of the bulbocavernosus and urethro-urethral sphincter reflex recorded from a patient

before operation are demonstrated in Fig. 1. Patient profiles after operation are summarized in Table 1. Eleven patients revealed voiding dysfunction after operation and no patient presented any evidence of local recurrence at the time of follow-up examination.

Patients studied were divided into two groups by results of postoperative UDS studies as shown in Table 2. In the normal voiding function group all postoperative indexes, including sensory thresholds of both the penile skin and the posterior urethra and latencies of the bulbocavernosus and urethro-urethral sphincter reflex, were on the levels of controls. Eleven patients with voiding dysfunction revealed normal levels of sensory threshold of the penile skin and latency of the bulbocavernosus reflex. In contrast, sensory threshold of the posterior urethra increased significantly and the urethro-

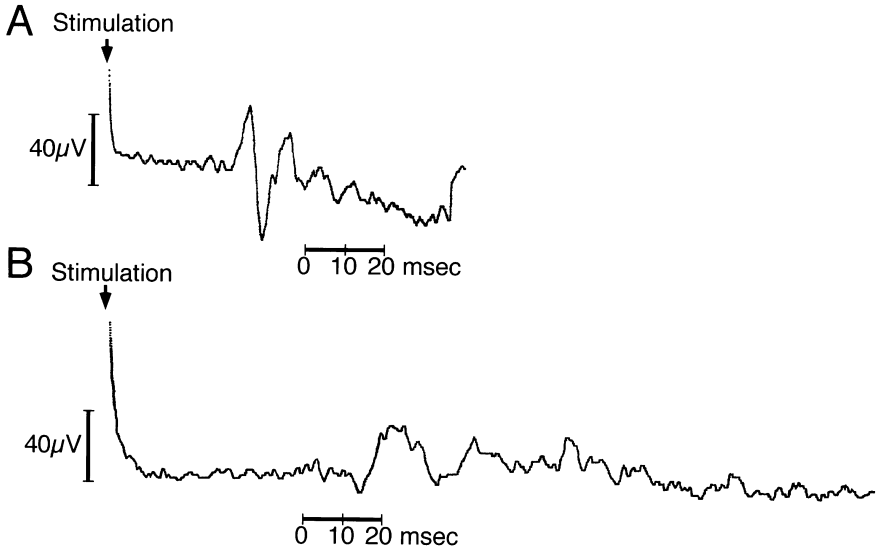

Fig. 1 Representative profile of the bulbocavernosus reflex (1A) and the urethro-urethral sphincter reflex (1B)

Table 1 Patient profiles after operation. *BCR* the bulbocavernosus reflex, *UUR* the urethro-urethral sphincter reflex, postoperative voiding dysfunction was caused by acontratile detrusor or detrusor underactivity in all cases, no patients revealed hydronephrosis at the end of follow-up

Patient no.	Dukes staging	Postoperative voiding dysfunction[a]	Sensory threshold (mA)		Latency of sacral reflex (ms)		Voiding dysfunction at follow-up[b]
			Penile skin	Posterior urethra	BCR	UUR	
1	A	No	1.6	4.5	33.6	63	
2	A	No	2	7.8	34	68	
3	B	No	2.4	5	26.8	53.5	
4	B	No	1.2	7	36.4	78	
5	B	No	4.5	9	34	75	
6	B	No	2.2	3.7	43.6	60	
7	B	No	2.3	6.7	33.6	64	
8	C	No	1.4	2	28	53	
9	C	No	1.5	7	25.6	74	
10	D	No	1.7	5	42.4	88	
11	D	No	2.1	11	39.2	60	
12	D	No	2	4.5	41.2	60	
13	D	No	2.2	8.3	31.2	65	
14	A	Yes	2.4	3.3	46	60.4	Absence (6)
15	A	Yes	3.2	9	37.2	66	Absence (6)
16	B	Yes	2.8	5	30.4	60	Absence (7)
17	B	Yes	2.2	18	29.6	67	Absence (7)
18	C	Yes	2.3	5	28	61	Absence (7)
19	A	Yes	2.8	25	34.4	Not evocable	Presence (12)
20	A	Yes	2	40	33.6	Not evocable	Presence (12)
21	A	Yes	3	20	38	Not evocable	Presence (11)
22	C	Yes	2	17	33.2	83	Presence (7)
23	C	Yes	1.4	28	27	56	Presence (12)
24	C	Yes	2	50	33.2	Not evocable	Presence (7)

[a] Voiding dysfunction confirmed by cystometry and uroflowmetry 1–3 months after operation

[b] Presence or absence of voiding dysfunction at the follow-up examination after operation. Follow-up periods are indicated as months in parenthesis. Voiding dysfunction recovered within 7 months of operation in all five patients

urethral sphincter reflex disappeared in four patients while latency of the urethro-urethral sphincter reflex was unchanged in the remaining seven in whom the urethro-urethral sphincter reflex was evoked.

Relation of postoperative sensory thresholds to voiding dsyfunction

Normal upper limits of sensory threshold were defined as the mean of corresponding control values plus two standard deviations. As shown in Table 3, postoperative sensory threshold of the penile skin was increased in one patient in the normal voiding function group and the voiding dysfunction group. The threshold of the posterior urethra was increased in 1 to 13 patients with normal voiding function and in 7 of 11 patients with voiding dysfunction including four whose the urethro-urethral sphincter reflex disappeared after surgery. Postoperative sensory thresholds of the posterior urethra were significantly related to postoperative voiding function ($P < 0.01$). In the normal voiding function group, each patient with increased sensory threshold of the posterior urethra or the penile skin had no apparent voiding dysfunction. The one with voiding dysfunction and increased sensory threshold of the penile skin had normal sensory threshold of the posterior urethra and his voiding function had recovered at follow-up examination.

Relation of postoperative sensory threshold of the posterior urethra to recovery of voiding dysfunction at follow-up examination

Follow-up UDS was performed to 11 patients with postoperative voiding dysfunction. As shown in Table 4, voiding function was recovered in all four patients with normal postoperative sensory threshold of the posterior urethra, while voiding function recovered in only one of seven with increased postoperative sensory threshold of the posterior urethra. Postoperative sensory thresholds of the posterior urethra significantly related to recovery or nonrecovery of voiding dysfunction ($P = 0.0152$) in those with postoperative voiding dysfunction. In seven patients whose postoperative sensory thresholds of the posterior urethra were increased voiding dysfunction recovered in none of four patients with diminished postoperative urethro-urethral sphincter reflex, and in only one of three patients even though the urethro-urethral sphincter reflex was evocable postoperatively

Table 2 Sensory threshold of the penile skin and the proximal urethra and latency of the bulbocavernosus and urethro-urethral sphincter reflex before and 1–3 months after the surgery. *BCR* bulbocavernosus reflex, *UUR* urethro-urethral sphincter reflex

	Control		Postoperative voiding dysfunction by UDS			
			No		Yes	
	n	Mean ± SD (range)	*n*	Mean ± SD (range)	*n*	Mean ± SD (range)
Sensory threshold (mA)						
Penile skin	25	1.9 ± 0.6 (1.2–3.5)	13	2.1 ± 0.8 (1.2–4.5)	11	2.4 ± 0.5 (1.4–3.2)
Posterior urethra	24	5.6 ± 1.8 (3.0–10.0)	13	6.4 ± 2.5 (2.0–11)	11	20.0 ± 15.0* (3.3–50)
Latency (ms)						
BCR	23	33.3 ± 4.2 (26.8–42.8)	13	34.6 ± 5.8 (25.6–43.6)	11	33.7 ± 5.4 (27.0–46.0)
UUR	20	65.0 ± 9.3 (46–80)	13	66.2 ± 10.1 (53–88)	7 4	64.8 ± 8.9 ∞[a] (60–83)

*$P < 0.05$, Mann-Whitney U test
[a] The urethro-urethral sphincter reflex was not evoked by the stimulation of 60 mA or more

Table 3 Number of patients having normal or increased sensory threshold of the penile skin and the posterior urethra 1–3 months after surgery

Postoperative voiding dysfunction	Number of patients	Sensory threshold			
		Penile skin		Posterior urethra	
		Normal	Increased	Normal	Increased
No	13	12	1	12	1
Yes	11	10	1	4	7

Increased sensory threshold of the penile skin and the posterior urethra indicated values higher than the mean of controls plus two standard deviations, namely higher than 3.1 mA and 9.1 mA, respectively. Sensory thresholds of the posterior urethra were significantly related to voiding function ($P < 0.01$) by Fisher's exact test

Disscussion

Eleven patients revealed postoperative voiding dysfunction by acontractile detrusor or detrusor underactivity during voiding, indicating the presence of impaired pelvic nerves. The averaged postoperative sensory threshold of the posterior urethra in these patients was significantly increased while that of the penile skin was on the control level. The findings indicate presence of the afferent nerve pathway from the posterior urethra through pelvic plexus. It has been reported [16] that profiles of cerebral potentials evoked by penile stimulation are similar to those evoked by stimulation of the anterior urethra and different from those evoked by stimulation of the posterior urethra or the bladder neck. These findings also confirm the difference of the sensory pathway of the posterior urethra and the penile skin.

The latency of the urethro-urethral sphincter reflex is found to be approximately twice as long as the bulbocavernosus reflex in all patient groups. The latencies of the urethro-urethral sphincter reflex and bulbocavernosus reflex in normal subjects have been reported as 40–84 ms [4, 6–8, 18] and 20–45 msec [2–5, 10, 14], respectively. As shown in Fig. 2, the reflex arc of the urethro-urethral sphincter reflex passes the pelvic plexus, the sacral cord and pudendal nerve, while that of the bulbocavernosus reflex passes the pudendal nerve, the sacral cord and the pudendal nerve. Therefore, different latencies of the urethro-urethral sphincter and bulbocavernosus reflex appear to result from two mechanisms; sensory afferents in the pelvic nerve belong to A delta and C fibers in which conduction velocity is slower than that of the pudendal nerve [19], and the intraspinal pathway of the urethro-urethral sphincter reflex is possibly more multisynaptic than that of the bulbocavernosus reflex [15, 18]. The previous and current results are consistent with the theory that the urethro-urethral sphincter reflex consists of the autonomic and somatic nerve systems and bulbocavernosus reflex consists of the somatic nerve system only.

The urethro-urethral sphincter reflex was evoked in 7 of 11 patients with postoperative voiding dysfunction with the latency of the urethro-urethral sphincter reflex on control levels. The findings suggest that partial impairment of the pelvic nerves, which causes detrusor dysfunction, does not necessarily cause delay of afferent signals. Anten et al. [3] found the urethro-urethral sphincter reflex delayed in 37% of diabetics and could not be generated in 3%. Koldewijn et al. [10] reported that the urethro-urethral sphincter reflex was delayed in 11% of cervical or thoracic spinal cord injuries and could not be evoked in 23%. Therefore it seems that the urethro-urethral sphincter reflex is delayed or not evocable in diabetic neuropathy and spinal cord injury. On the other hand our results suggest that the urethro-urethral sphincter reflex is an all-or-nothing phenomenon after pelvic nerve injury and unevocability of the urethro-urethral sphincter reflex possibly means complete disruption of the pelvic nerve.

Among 11 patients with postoperative voiding dysfunction, an unchanged postoperative sensory threshold of the posterior urethra and the disappearance of an evoked urethro-urethral sphincter reflex were found to relate significantly to later recovery or nonrecovery of voiding dysfunction, respectively. Although preoperative voiding function has not been confirmed in all of the above 11 patients, it appears most likely from the cur-

Table 4 Relation of sensory threshold of the posterior urethra 1–3 months after the surgery for recovery of voiding dysfunction more than 6 months after the surgery

Sensory threshold of posterior urethra	Voiding dysfunction at follow-up		Total
	Recovered	Unrecovered	
Normal	4	0	4
Increased	1	6	7
Total	5	6	11

$P = 0.0152$, Fisher's exact test

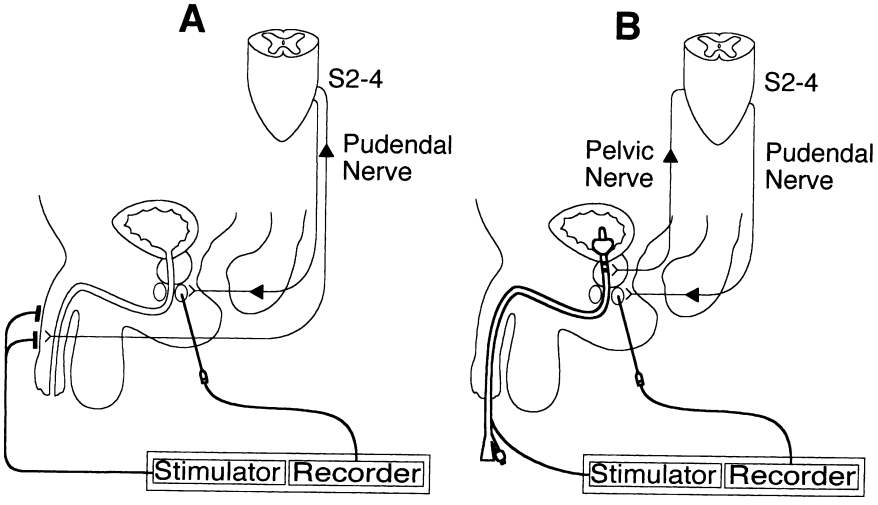

Fig. 2 Diagram of the anatomical basis of the sacral reflex and the position of electrodes used for stimulation and recording. (A) the bulbocavernosus reflex and (B) the urethro-urethral sphincter reflex

rent results that increase of sensory threshold of the posterior urethra indicates serious dysfunction of the pelvic nerves that is difficult to recover. And it is also likely that the sensory threshold of the posterior urethra is a better functional test for pelvic nerve injury than evoked potential of the urethro-urethral sphincter reflex.

In conclusion, postoperative evaluation of the sensory threshold of the posterior urethra is useful in evaluating pelvic nerve injury. Postoperative voiding dysfunction may continue in those in whom evoked urethro-urethral sphincter reflex has disappeared and can be expected to recover in those with normal levels of postoperative sensory threshold of the posterior urethra.

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