The Role of Membranous Urethral Afferent Autonomic Innervation in the Continence Mechanism After Nerve Sparing Radical Prostatectomy: A Clinical and Prospective Study

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Purpose: We evaluated the somatic and autonomic innervation of the pelvic floor and rhabdosphincter before and after nerve sparing radical retropubic prostatectomy using neurophysiological tests and correlated findings with clinical parameters and urinary continence.

Materials and Methods: From February 2003 to October 2005, 46 patients with prostate cancer were enrolled in a controlled, prospective study. Patients were evaluated before and 6 months after nerve sparing radical retropubic prostatectomy using the UCLA-PCI urinary function domain and neurophysiological tests, including somatosensory evoked potential, and the pudendo-urethral, pudendo-anal and urethro-anal reflexes. Clinical parameters and urinary continence were correlated with afferent and efferent innervation of the membranous urethra and pelvic floor. We used strict criteria to define urinary continence as complete dryness with no leakage at all, not requiring any pads or diapers and with a UCLA-PCI score of 500. Patients with a sporadic drop of leakage, requiring up to 1 pad daily, were defined as having occasional urinary leakage.

Results: Two patients were excluded from study due to urethral stricture postoperatively. We evaluated 44 patients within 6 months after surgery. The pudendo-anal and pudendo-urethral reflexes were unchanged postoperatively ($p = 0.93$ and 0.09, respectively), demonstrating that afferent and efferent pudendal innervation to this pelvic region was not affected by the surgery. Autonomic afferent denervation of the membranous urethral mucosa was found in 34 patients (77.3%), as demonstrated by a postoperative increase in the urethro-anal reflex sensory threshold and urethro-anal reflex latency ($p < 0.001$ and 0.0007, respectively). Six of the 44 patients used pads. One patient with more severe leakage required 3 pads daily and 23 showed urinary leakage, including 5 who needed 1 pad per day and 18 who did not wear pads. Afferent autonomic denervation at the membranous urethral mucosa was found in 91.7% of patients with urinary leakage. Of 10 patients with preserved urethro-anal reflex latency 80% were continent.

Conclusions: Sensory and motor pudendal innervation to this specific pelvic region did not change after nerve sparing radical retropubic prostatectomy. Significant autonomic afferent denervation of the membranous urethral mucosa was present in most patients postoperatively. Impaired membranous urethral sensitivity seemed to be associated with urinary incontinence, particularly in patients with occasional urinary leakage. Damage to the afferent autonomic innervation may have a role in the continence mechanism after nerve sparing radical retropubic prostatectomy.

Key Words: prostate, prostatic neoplasms, prostatectomy, reflex, innervation

A significant decrease in UI has been achieved after the Walsh and Donker description of NSRRP.[1] However, UL after radical prostatectomy has a profound impact on patient quality of life and it still occurs in 8% to 87% of patients, depending mostly on the definition of UI.[2] Most studies have focused on the incidence of UI after prostatectomy but its etiology is not always well addressed.

NSRRP interferes with the anatomy and function of the urethral sphincter complex. Because urinary continence after surgery relies on the remaining sphincteric complex, it must be preserved to avoid leakage.[3] However, this cannot guarantee a continent status in all patients. After NSRRP it is not uncommon that patients present with minor UL and OUL.[4] Nevertheless, most studies have only considered incontinent patients using more than 1 pad per day, assuming that 1 pad per day should be acceptable. To our knowledge there is no consensus on the physiopathology of post-NSRRP UI, particularly in cases of minor leakage. Some study has been done to test the pelvic innervation without completely elucidating the basis of UI after NSRRP.[5,6] It is more likely that continent or incontinent status after NSRRP is not only due to direct trauma or damage to the rhabdosphincter, but also to a more complex physiopathological mechanism.[7–9]

NPT is an objective and reliable method of measuring afferent and efferent nerve conduction and integrity.[7–9] Therefore, it might provide information on the somatic and autonomic pelvic innervation that is compromised by

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NSRRP and the role of neurological impairment. We prospectively applied several methods of NPT to establish and characterize possible alterations in the pelvic and membranous urethral afferent and efferent innervation caused by NSRRP as well as the role of neurological impairment in urinary continence.

MATERIALS AND METHODS

Study Design and Patients

The study was performed in accordance with institutional ethics committee approval. From February 2003 to October 2005, 46 consecutive patients with organ confined prostate cancer (stages T1 and T2) who were scheduled for NSRRP were prospectively enrolled in the study. Those with previous pelvic irradiation, a history of pelvic surgery, transurethral surgery or trauma, neuropathic drug use, alcohol abuse and systemic or neurological disease that could interfere with the pelvic innervation were excluded from study. Mean patient age was 63.7 years (range 41 to 79). Table 1 shows relevant patient characteristics.

Patients were evaluated preoperatively and 6 months postoperatively using the urinary function domain of UCLA-PCI[10] (5 questions with a total score of 0 to 500 with the lower the score, the worse the continence), IIEF-5, International Prostate Symptoms Score and neurophysiological tests, including SSEP, PUR, PAR and UAR.[11] Neurophysiological evaluation was performed using Neuropack Sigma electroneuromyographic instruments (Nihon-Kohden, Tokyo, Japan).

Somatosensory Evoked Potential

A cortical response can be readily recorded following stimulation of the pudendal nerve. Stimulation was performed by a bipolar handheld surface electrode placed on the proximal dorsal aspect of the penis with the cathode proximal and anode distal using square wave pulses with a duration of 0.2 millisecond at a frequency of 4.7 Hz. The sensitive threshold was defined as the lowest current perceptible at the stimulation point. To record stable cortical SSEPs it was necessary to use an intensity equivalent to 3 times the threshold. Cortical responses were recorded by silver 10 mm surface electrodes at Cz′-Fz in the midline of the scalp and at the P3–P4 positions with a ground electrode between Cz′-Fz according to the International 10–20 system of electrode placement. A total of 500 stimuli were delivered and the response was amplified, averaged and recorded. Three tracings were superimposed to determine the consistency of the response. Latency was determined at the onset of the first positive response (P1 or P40).

TABLE 1. *Preoperative patient demographics*

Characteristic	No. Pts (%)
Overall	46 (100)
Ethnicity:	
White	42 (91.3)
Black	4 (8.7)
Gleason score:	
2–5	9 (19.6)
6	17 (36.9)
7–10	20 (43.5)
Continence	46 (100)
IIEF-5 erectile dysfunction:	
Absent	39 (84.8)
Mild	5 (10.9)
Moderate	0
Severe	2 (4.3)
International Prostate Symptom Score:	
0–7	39 (84.8)
8–20	7 (15.2)
21–35	0
Body mass index (kg/m^2):	
Less than 20	3 (6.5)
20–25	18 (39.1)
26–30	21 (45.6)
Greater than 30	4 (8.7)
Prostate specific antigen (ng/ml):	
0–4.0	5 (10.9)
4.1–10.0	28 (60.9)
Greater than 10.0	13 (28.3)
Prostate wt (gm):	
Less than 51	33 (71.7)
Greater than 50	13 (28.3)

Pudendo-Urethral Reflex

The reflex was elicited by stimulating the dorsal nerve of the penis and recording it with an intraurethral surface electrode. A ground electrode was placed at the right thigh. The sensitive threshold was determined and double pulse, square wave stimuli were applied to dorsal base of the penis by a bipolar handheld surface electrode. Stimulus duration was 0.2 millisecond, an irregular frequency less than 0.5 Hz was used, and intensity was standardized at 15, 20 and 25 mA with 4 stimuli per intensity grade. Recordings were done using a 21L0111 platinum bipolar ring surface electrode (Medtronic, Minneapolis, Minnesota) mounted 2.5 cm below the balloon on a 10Fr Foley catheter and inserted into the bladder using aseptic technique. Under digital rectal examination guidance the electrode was located at the level of the external urethral sphincter to record its activity. A 20 and a 10 Hz filter was used for low and high frequency recording, respectively.[11]

Pudendo-Anal Reflex

For this reflex the same stimuli and recording parameters were used as described for PUR, although external anal sphincter recordings were made using 3 silver 10 mm surface electrodes situated at the 3, 6 and 9 o'clock positions in the mucocutaneous transition line of the anus. The active electrodes were at the 3 and 9 o'clock positions, and the reference electrode was at the 6 o'clock position.

Urethro-Anal Reflex

From the bipolar electrode around the Foley catheter, as described to record PUR, the generated stimulus duration was 0.2 millisecond with an irregular frequency of less than 0.5 Hz and intensity standardized at 15, 20 and 25 mA with 4 stimuli per intensity grade. Data were recorded using the same electrodes already located in the mucocutaneous transition line of the anus for PAR, including the sensitive threshold at the membranous urethral level and stimulus latency time.

Technical Considerations

PUR, PAR and UAR latency was considered the time elapsed between the stimulus and the first answer (R1). We used rigorous criteria to define urinary continence as complete dryness requiring no pads or diapers and with presenting no leakage and a UCLA-PCI score of 500. Patients with sporadic drops of leakage requiring up to 1 pad per day were