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Assessment of changes in penile sensation by electrophysiological study after radical prostatectomy: A pilot study

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Abstract

Background: To evaluate the changes in penile sensation by electrophysiological tests in patients who underwent radical prostatectomy (RP) and to demonstrate the role of dorsal penile nerve injury in postoperative erectile dysfunction.

Materials and methods: Twenty-six volunteer patients who were eligible for RP were included in the study. Preoperative penile sensory electromyography and the International Index of Erectile Function-5 (IIEF-5) questionnaire were done for each patient. Erectile function assessment and electrophysiological evaluation of penile sensation were repeated at postoperative 3rd and 6th months.

Results: Postoperative IIEF-5 scores and electromyography values were significantly lower than preoperative findings ($p < 0.05$). The IIEF-5 scores in the nerve sparing-RP (NS-RP) group were significantly higher than the non-nerve sparing-RP (NNS-RP) group in the postoperative period. Nerve conduction velocity values in the NS-RP group were also higher than the NNS-RP group at the postoperative 3rd and 6th months. However, these changes were not statistically significant ($p > 0.05$).

Conclusions: Patients who underwent RP have decreased penile sensation due to cavernous nerve damage and a possible dorsal penile nerve injury. The decrease of penile sensation may be associated with postoperative erectile dysfunction.

Keywords: Dorsal penile nerve; Erectile dysfunction; Penile sensation; Prostate cancer; Radical prostatectomy

1. Introduction

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related mortality among men in the United States.[1] Radical prostatectomy (RP) has been the standard surgical treatment for clinically localized prostate cancer,[2] but erectile dysfunction (ED) is among the long-term complications of this surgical modality. ED can have very high rates (up to 100%) in initial periods after RP in bilateral non-nerve-sparing patients.[3] The causes of postoperative ED are surgeon's inexperience, improper surgical technique, accessory pudental artery injury, and damage of the neurovascular bundle.[4,5]

Erection occurs in 3 ways, as genital stimulation (contact and reflexogenic), central stimulation (without contact or psychogenic), or central nervous system stimulation (nocturnal).[6] The dorsal penile nerve (DPN) carries the sensory innervations from the penis shaft and the glans. Therefore, it has an important role in tactile stimulated erection.[7] Sensorial electromyography (EMG) to the DPN has shown that sensory disorders in the distal penis occur in the early period.[8] Cadaver dissections demonstrated that the DPN is located very close to the prostate apex. The close route of this nerve to the prostatic apex may cause injury during RP.[9]

In this study, we aimed to evaluate the changes in penile sensation by the electrophysiological test in patients who underwent RP and to demonstrate the role of DPN injury in postoperative ED.

2. Materials and methods

The study was designed as a prospective, controlled study. After the approval of the ethics committee, 26 volunteer patients who were eligible for RP were included in the study. The study was carried out in the University of Health Sciences Antalya Training and Research Hospital and the duration of the study was 1 year. Those with any neurological disease (peripheral neuropathy, diabetic neuropathy, history of cerebrovascular disease, peyronie, or congenital penile malformation), with a history of pelvic radiotherapy or pelvic surgery were excluded. None had neoadjuvant androgen deprivation therapy. There was no cut-off age for the enrolled patients to the study. Patients were evaluated with a detailed physical examination and anamnesis. Routine blood tests (complete blood count, biochemical analysis, prostate specific antigen, and full automated urinalysis) were performed. Each patient underwent a robot-assisted laparoscopic

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RP which was performed by a single surgeon. When the nerve-sparing technique was done, it was always bilaterally performed. Preoperative penile sensory EMG and the International Index of Erectile Function-5 (IIEF-5) questionnaire were done for each patient. Erectile function assessment and electrophysiological evaluation of penile sensation were repeated at the postoperative 3rd and 6th months. The main point of the evaluation was the erectile function, studied with the IIEF-5.

Electrophysiological studies were performed in the morning between 9 and 10 AM, in a quiet room with a temperature of 23–25°C, while the person was in the supine position, with loose clothing and awake. A two-channel electroneuromyography device (Nihon-Kohden-Neuropack, model MEB-2200) was used for the studies and the penile EMG was performed by the Clawson method.[10] The penis was placed in the concave side of the specially designed orthoplast penile traction device and stretched to reach its maximum length by pulling from the glans. A Cunningham incontinence clamp was placed on the glans and the glans continued to be held while the penis was stretched. EMG paste was used to place active and reference steel electrodes. The active recording electrode was placed as close as possible to the proximal part of the penis. The reference electrode was placed 4 cm above the active electrode. The proximal part of the penis was orthodromically stimulated with the active electrode and the dorsal glans was stimulated with the reference electrode. Nerve conduction velocity (NCV), amplitude, and latency values measured during EMG were recorded.

The data were expressed as mean and median (minimum–maximum) for numeral variables and as frequencies and percentages for categorical variables. The distribution of the variables was measured by the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to analyze the quantitative independent data. The Wilcoxon test was used to analyze the dependent quantitative data. The effect level and cut-off value were investigated with a receiver operating characteristic curve. The SPSS 22.0 program was used in the analysis and $p < 0.05$ was considered significant.

3. Results

A total of 26 patients who matched the defined criteria were included in the study. Demographic data and clinical features of the patients are shown in Table 1. The mean age of the patients was 63.7 years (range 51–74 years), in which 16 were 65 or older and 18 patients had no or mild preoperative ED. NS-RP was performed in 15 patients and NNS-RP surgery was performed in 11 patients. Although 18 patients had no or mild ED, NS-RP was performed only in 15 patients. Three of the patients were in the high-risk group and 13 of the patients used PDE-5 inhibitors after RP. The rest of the patients did not undergo any postoperative rehabilitation for ED. We compared the 2 groups (nerve sparing and non-nerve sparing) in order to evaluate if the groups had any difference in terms of patients' demographic and baseline characteristics. We found that there was no statistically significant difference between the 2 groups (Table 2). Preoperative EMG values and IIEF-5 scores of the patients are shown in Table 3. Postoperative IIEF-5 scores and EMG values were significantly lower than preoperative findings ($p < 0.05$). Although an increase in NCV values was observed in the postoperative 3rd month, this increase was not statistically significant ($p > 0.05$). IIEF-5 scores and NCV values of the patients who underwent NS-RP or NNS-RP were compared in Table 4. There was a significant difference between NS-RP and NNS-RP groups ($p < 0.05$). The IIEF-5 scores in the NS-RP group were significantly higher than in the NNS-RP group in the postoperative period. NCV values in the NS-RP group were also

Table 1

Patient characteristic.

Variable	Results
Age, years	63.7 (51–74)
Nerve sparing surgery, *n*	15 (57.7%)
Tadalafil intake, *n*	13 (50%)
Pathological stage, *n*	
T2a	5 (19.2%)
T2c	12 (46.2%)
T3a	5 (19.2%)
T3b	4 (15.4%)
Comorbidity, *n*	
Diabetes mellitus	2 (7.7%)
Hypertension	13 (50%)
Coroner artery disease	10 (38.5%)

Table 2

Comparison of demographics and baseline characteristics of non-nerve sparing and nerve sparing groups.

Variable	Non-nerve sparing group ($n=11$)	Nerve sparing group ($n=15$)	*p*
Age, years	66 (52–74)	59 (51–71)	0.10
Pre IIEF-5 score	17 (5–25)	20 (10–25)	0.49
Diabetes mellitus, *n*	0	2	0.14
Coronary artery disease, *n*	4	3	0.49
Hypertension, *n*	4	8	0.40
Pathological stage, *n*			
T2	6	11	0.32
T3	5	4	0.28

IIEF-5 = International Index of Erectile Function-5.

Table 3

Comparison of IIEF-5 scores and EMG values before and after operation.

	Range	Mean ± SD	*p*
IIEF-5 Score			
Preoperation	5–25	17.8 ± 6.4	
Postoperation 3 month	5–22	6.7 ± 4.0	0.000*
Postoperation 6 month	5–23	7.9 ± 5.6	0.000*
Latency, ms			
Preoperation	1–3	2.2 ± 0.5	
Postoperation 3 month	0–5	0.9 ± 1.5	0.001*
Postoperation 6 month	0–3	1.2 ± 1.2	0.002*
Amplitude, mV			
Preoperation	2–9	4.3 ± 2.0	
Postoperation 3 month	0–17	1.8 ± 4.0	0.003*
Postoperation 6 month	0–11	3.0 ± 3.4	0.045*
NCV, m/s			
Preoperation	15–65	34.8 ± 13.8	
Postoperation 3 month	0–40	8.4 ± 13.7	0.000*
Postoperation 6 month	0–68	22.2 ± 22.9	0.041*

EMG = electromyography; IIEF-5 = International Index of Erectile Function-5; NCV = nerve conducting velocity.
* $p < 0.05$.

Table 4

Comparison of IIEF-5 scores and EMG values before and after operation in NS-RP and NNS-RP patients.

	Nerve sparing (–)	Nerve sparing (+)	*p*
IIEF-5 score	Mean±SD	Mean±SD	
Preoperation	15.4±7.6	19.5±4.8	0.144*
Postoperation 3 month	5.1±0.3	7.9±4.9	0.016*
Preoperation/3 month *p*	0.012†	0.001†	
Postoperation 6 month	5.0±0.0	10.0±6.7	0.020*
Preoperation/6 month *p*	0.012†	0.001†	
NCV, m/s			
Preoperation	40.6±13.6	30.5±12.7	0.052*
Postoperation 3 month	4.5±10.2	11.2±15.6	0.204*
Preoperation/3 month *p*	0.006†	0.015†	
Postoperation 6 month	22.0±22.6	22.3±23.9	0.935*
Preoperation/6 month *p*	0.091†	0.211†	

EMG = electromyography; IIEF-5 = International Index of Erectile Function-5; NCV = nerve conducting velocity; NNS-RP = non-nerve sparing-radical prostatectomy; NS-RP = nerve sparing-radical prostatectomy.
* Mann-Whitney *U* test.
† Wilcoxon test.

higher than in the NNS-RP group at postoperative 3rd and 6th months. However, these changes were not statistically significant ($p > 0.05$).

4. Discussion

RP is considered the gold standard treatment for localized prostate cancer.[11] Although long-term results are good, the rate of postoperative ED was reported to be 14%–90% depending on the surgical approach and the surgeon's experience.[12–14] In addition, Boylu et al.[15] reported that the rate of ED after robot-assisted laparoscopic RP was 83% in the 12th month. Neuropraxia is the most common cause of postoperative ED in patients undergoing RP.[14] After the surgery, ischemia and local inflammation are observed in tissues due to cutting, coagulating, and retraction to better see the operative field. These changes affect the cavernous nerves (CNs) and reduce local oxygenation. As a result, pro-apoptotic and pro-fibrotic changes in the corpora cavernosum are considered responsible for the formation of RP related ED.[12,13] Autonomic fibers are carried to the penis by the CN which has a positive neural nitric oxide synthase activity.[16,17] Some anastomosing fibers are between terminal CNs and the DPN, below the pubic arch in the penile hilum region.[18] After anastomosis, DPN fibers also show positive neural nitric oxide synthase activity. The presence of this activity suggests that CNs use the DPN in transporting autonomic fibers distal to the corpus cavernosum and this probably helps to achieve erection.[19] In addition, the DPN assists the transport of the afferent branch of the bulbocavernosus reflex to provide normal erection and ejaculation.[20,21] While the CN adjacent to the prostate capsule is usually damaged during RP, it is unlikely to injure the pudendal nerve that passes through the Alcock's canal which is just below the levator muscles.[22] However, Narayan et al.[9] reported that the DPN is very close to the prostate apex and can be thermally damaged during apex dissection in RP. Although the somatic sensory afferents of the penis and perineum are generally carried by the pudendal nerve, the autonomic afferents of the penis are carried by CNs.[23] However, this is not precisely defined. In the study of Yiou et al.,[24] it was found that the penile thermal sensorial threshold was significantly increased in patients who underwent NNS-RP compared with patients who underwent NS-RP. This result shows that penile sensorial fibers can be found in CNs.

The most commonly used test to assess autonomic nerve fibers of the penis is the recording of penile sympathetic skin responses to electrical stimulation. However, the amplitude of the response measured in this test limits its usage.[25] Measurement of penile thermal sensation thresholds is another method used to demonstrate ED due to damage in penile innervation.[26–28] Apart from these, NCV and amplitude values measured by sensorial EMG of the DPN were found to show the sensory disorders of the distal penis in the early period.[8] In our study, we measured the sensory nerve conduction of the DPN by performing EMG in our patients to evaluate the penile sensation.

When compared with the preoperative period, we found a significant decrease in NCV of the DNP in the postoperative 3rd and 6th months in patients who underwent RP ($p < 0.05$). We also observed the decreased IIEF-5 scores in the postoperative period and they were statistically significant ($p < 0.05$). Considering both together, we think that the penile sensation can be adversely affected during RP. We also believe that this damage may be associated with ED due to RP because the afferent sensory nerve fibers of the penis can join the pudendal nerve and the CNs. Accordingly, as shown by Yiou et al.,[24] changes in penile sensation after RP may be associated with ED.

In the NS-RP group, the IIEF-5 scores in the postoperative 3rd and 6th months were significantly higher than in the NNS-RP group ($p < 0.05$). In addition, there was a decrease in IIEF-5 scores for both groups compared with the preoperative period and this decrease was statistically significant ($p < 0.05$). When the NCV values obtained by EMG were compared for these 2 groups, a significant decrease was observed in the postoperative period in both groups ($p < 0.05$). Although postoperative NCV values were higher in the NS-RP group than in the NNS-RP group, this was not statistically significant ($p > 0.05$). Taken together, we think that the decrease in penile sensation in patients who underwent NS-RP can be caused by thermal damage of the DPN during the apex dissection of the prostate due to its closeness to the apex.

In contrast, there was an increase in NCV values in the postoperative 6-month compared with 3-month in both groups, but this was not statistically significant ($p > 0.05$). Chen et al.[29] reported that after damaging bilateral CNs in a rat model, the number of minor branches of the DPN significantly decreased just after the injury. However, they reported an increase in the number of minor branches at the 28th day after the injury and this indicates that nerve regeneration started in the early period after CN injury. In addition, some nerve fibers were macroscopically observed lateral to the original site of the neurovascular bundle. The CNs may form a network of nerve fibers, and some can be incidentally preserved even if the main neurovascular bundle is macroanatomically resected.[30] Takenaka et al.[31] identified accessory neural pathways around the prostate apex and urethral sphincter in 42% of patients. Both studies supported that these pathways and interconnections between nerve fibers might help to explain the potency recovery after neurovascular bundle damage. However, more long-term studies are needed to prove this.

There were some limitations of this study. First, we completed this study with 26 patients. Second, we followed-up patients for 6 months in the postoperative period. In future studies, the length of follow-up should be longer in order to better observe the regeneration of nerves.

5. Conclusion

Patients who underwent RP had a decreased penile sensation due to CN damage and a possible DPN injury. The decrease of penile sensation may be associated with postoperative ED. More studies can help to clarify this issue.

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Statement of ethics

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study protocol was reviewed and approved by the Institutional Review Board of Health of the Science University Antalya Training and Research Hospital (approval No: 2/6). Informed consent was obtained from all subjects when they were enrolled.

Conflict of interest statement

No conflict of interest has been declared by the author.

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Conception and Design: AY, EI, MY
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Provision of study materials or patients: AY, IE, TC and MS
Collection and Assembly of data: MA, KK, MS
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