Nerves in the Areas Posterior to the Prostate Base Contribute to Erectile Function: An Intraoperative Electrical Stimulation Assessment

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OBJECTIVE To confirm the distribution of functional nerves involved in erectile function at the posterior of the prostate base, intraoperative nerve stimulation was performed during robot-assisted radical prostatectomy (RARP)

METHODS Several points at the posterior of the prostate and the posterolateral typical neurovascular bundle (NVB) were electrically stimulated at the level of the prostate base during RARP in patients with clinically localized prostate cancer. The prostate pedicle (PP), medial side of the PP (MPP), Denonvilliers' fascia (DF), and typical NVB were stimulated using bipolar electrodes. The changes in pressure at the middle of the urethra were measured using an inserted balloon-catheter to detect the increase in cavernosal pressure.

RESULTS Although the study included only 12 patients, each stimulation of the PP, MPP, and NVB induced evident urethral pressure responses in all patients. The median amplitude of the pressure responses was 5.49 (IQR 3.11-8.42), 6.00 (IQR 3.70-8.30), and 3.22 (IQR 2.48-7.19) cm H_2O at the PP, MPP, and NVB, respectively. The amplitude of responses at the PP and MPP was not small compared with the responses at the typical NVB. Stimulations at the DF induced unstable weak urethral response alone or no response in all patients.

CONCLUSION We showed that electrostimulation of the PP and MPP increases the cavernosal pressure similar to the typical NVB stimulation. These findings indicate that maximal preservation of the tissues at the posterior area of the prostate base can contribute to optimal recovery of postoperative erectile function after nerve-sparing RARP. UROLOGY 132: 156−160, 2019.

The traditional concept that the nerve fibers responsible for erectile function run exclusively in the neurovascular bundle (NVB)[1] has been replaced by the recent concept of the periprostatic nerve network.[2-5] Functional nerve distribution spreading not only on the posterolateral side, but also on the lateral and ventral sides of the prostate has been well elucidated.[2] In contrast, the nerve distribution at the posterior of the prostate has not been established. Robot-assisted radical prostatectomy (RARP) has enabled us to visualize the posterior plane of the prostate during the usual base-to-apex dissection; however, further knowledge regarding fine and precise nerve distribution at the posterior area is still necessary. Histologic investigations identified many nerve fibers at the posterior of the prostate base.[6,7] Medical imaging studies have reported a nerve network spreading in the posterior and posterolateral areas of the prostate base, such as a neural hammock, in computer graphic images of the 3-dimensional reconstruction of serial histologic sections[8,9] or in magnetic resonance images analyzed with diffusion tensor imaging technique.[10]

Despite histologic and imaging investigations indicating that the nerve fibers were distributed in the posterior area, no functional investigations have been conducted to evaluate whether the nerve fibers distributed in these areas actually contribute to erectile function. Since the presence of nerve fibers does not necessarily indicate that they play a role in erection, it is necessary to obtain evidence to prove their role in erectile function. A suitable evidence proving their role in erectile function would be to show increased cavernosal pressure under electrical stimulation. Therefore, intraoperative nerve stimulation was performed during RARP to confirm the distribution

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of functional nerves involved in erectile function at the posterior of the prostate base.

MATERIALS AND METHODS

Intraoperative nerve stimulation was performed to confirm the distribution of the functional posterior nerves during RARP in patients with clinically localized prostate cancer. This study was approved by the Ethics Committee of the Tohoku Medical and Pharmaceutical University.

To perform electrical stimulations of the nerve fibers at the posterior of the prostate base, the prostate was lifted using the forth arm after resection of the vas deferens was completed, and the seminal vesicles were dissected. Subsequently, the Denonvilliers' fascia (DF) and the prostate pedicles (PPs) were observed under direct vision. The lateral margin of the DF was unclear because the DF fuses laterally to the lateral pelvic fascia and pararectal fascia.[11] Therefore, we defined the area of flat membranous structure to stimulate as the DF. The tissue on the medial side of the PP was defined as MPP. The MPP was the tissue located between the PP and DF (Fig. 1). We stimulated the PP, MPP, and DF in the posterior area of the prostate base using bipolar electrodes and compared responses obtained for the PP, MPP, and DF stimulations with those for the typical NVB stimulation at the level of the prostate base. Each electrostimulation was maintained for 30 seconds at 30 mA/10 Hz in a monophasic rectangular pulse with a pulse duration of 1.0 milliseconds in the same setting that in our previous study.[2]

Responses to electrical stimulation were observed as changes in urethral pressure in the middle portion of the penile shaft using an inserted 9 Fr balloon catheter filled with 1.5 mL of saline to detect the increase in cavernosal pressure.[12] The catheter was connected to a disposable pressure transducer set, and changes in pressure were recorded on a pen recorder to measure responses to stimulations. The manometry system was calibrated prior to use in each case. The amplitude, determined as the maximal pressure changes (cm H_2O) from the baseline in response to each stimulation, was measured from the recorded chart (Fig. 2). The median of the amplitude of the pressure response to each stimulation position of the posterior area, PP, MPP, and DF was calculated and compared with that of the typical NVB stimulations.

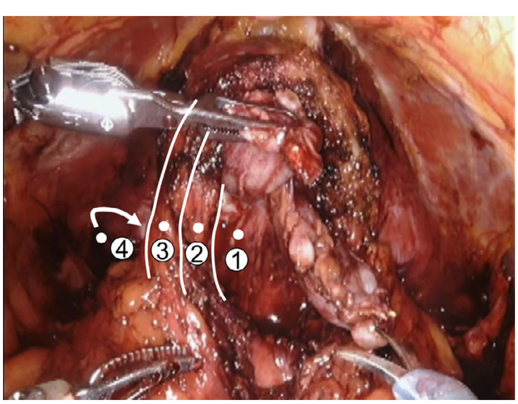

Figure 1. Electrostimulation points. Electrostimulation points (yellow dots) of the posterior area of the prostate base (1) the Denonvilliers' fascia, (2) medial side of the prostate pedicle, and (3) prostate pedicle, and (4) the typical neurovascular bundle. (Color version available online.)

Statistical Analysis

Data are expressed as median (IQR). Wilcoxon signed ranks test were used to compare amplitudes of pressure responses to each electrostimulation point. Values of $P < .05$ were considered statistically significant.

RESULTS

Intraoperative nerve stimulation was performed to confirm the distribution of the functional posterior nerves during RARP in 12 patients (median age, 69.5 years; IQR, 67.0-71.3 years) with clinically localized prostate cancer. Table 1 lists the clinical and pathologic characteristics of the patients. The stimulation of the PP, MPP, and NVB induced evident urethral pressure responses in all patients. The median amplitude of the pressure responses was 5.49 (IQR 3.11-8.42), 6.00 (IQR 3.70-8.30), and 3.22 (IQR 2.48-7.19) cm H_2O at the PP, MPP, and NVB, respectively. No significant differences were seen in the median amplitude of the pressure responses at the PP, MPP, and NVB. The amplitude of the responses at the PP and MPP was not small compared with the responses at the typical NVB (Fig. 3). Stimulations at the DF induced unstable weak urethral responses in 5 patients or no response in 7 patients, and the median amplitude of the pressure responses in 12 patients was 0.0 (IQR 0-0.47) cm H_2O.

DISCUSSION

In recent years, the surgical techniques for RARP have evolved, and increasing attention has been paid to preserve as many nerve fibers responsible for erectile function as possible. The traditional concept that the nerve fibers responsible for erectile function run exclusively in the NVB at the posterolateral area[1] has been replaced by the recent concept of the periprostatic nerve network.[2-5,13] In the era of open radical prostatectomy, intraoperative nerve stimulation can confirm the distribution of the functional nerves involved in erectile function at the ventral, lateral, and posterolateral side of the prostate[2] and at the rectal wall posterolaterally, apart from the typical NVB.[14] the recent era of RARP, because the posterior area of the prostate has always been well visualized during the usual base-to-apex dissection, knowledge of a more fine and precise nerve distribution at the posterior of the prostate is required in addition to the already known nerve distributions. However, to the best of our knowledge, the functional nerve distribution for erectile function at the posterior of the prostate has not previously assessed in humans. The present study reports that the nerve fibers in the PP and MPP at the posterior of the prostate base also contribute to erectile function together with the nerve fibers in the NVB at the posterolateral area of the prostate, as assessed by intraoperative nerve stimulation.

The nerve fibers in the area posterior to the prostate base are at risk of being injured when the DF is incised, and the posterior space of the prostate is enlarged laterally.

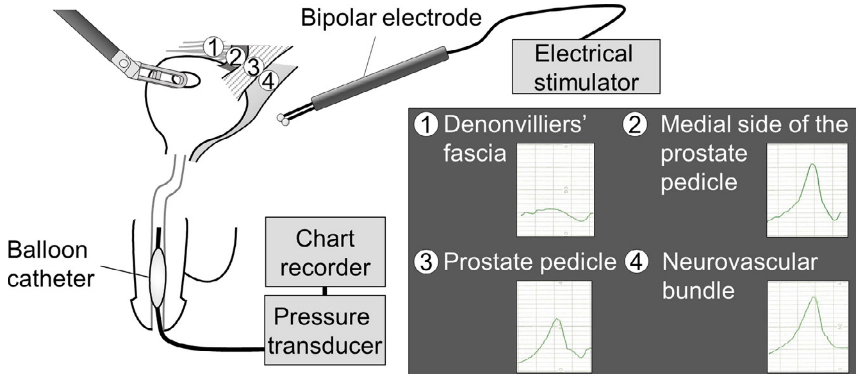

Figure 2. Electrostimulation and responses. Bipolar electrodes were used to stimulate each point at the posterior of the prostate base and the typical neurovascular bundle. Changes in pressure at the middle of the urethra were measured using an inserted balloon-catheter to detect increases in cavernosal pressure. The waveforms on the bottom right corner are representative traces of the urethral pressure responses to each electro-stimulation point.

We usually incise the DF at the start of the posterior dissection of the prostate.[15] While incising the DF, we should resect only the membranous structure of the DF, taking care not to cut into the PP and MPP, wherein the nerve fibers for erectile function are present. After incision of the membranous structure of the DF, the dissection line should be adjusted to the line between the prostate and lateral pelvic fascia to preserve as many posterior nerve fibers for erectile function as possible. We set 2 landmark points at the prostate surface just lateral to the seminal vesicle and the ventral circumference at the 10-o'clock position of the prostate, respectively. We routinely ensure that all periprostatic tissues at the lateral side of the dissection-line through the 2 landmark points during nerve-sparing RARP are preserved (Supplementary Fig. 1).

In this study, we could not have stable or obvious pressure responses at the DF stimulations compared with the other stimulations. Kourambas et al reported in their histologic study that certain nerve fibers were scattered throughout the DF although prominent nerve fibers were laterally within the fasciae at the junction of the DF with the lateral pelvic and pararectal fascia.[11] In contrast, Costello et al demonstrated in their anatomic study that NVB runs within the junction of the DF with the lateral pelvic and pararectal fascia.[16] Few nerve fibers have been presumed to run along the DF, and our low responses to the DF stimulations are consistent with the histologic and anatomic studies.

A counterargument to the responses to the electrostimulations at the PP and MPP may be proposed that functional nerve fibers for erectile function exist only in the already known parapelvic nerve network, including the typical NVB, and the responses induced by the PP and MPP stimulations were induced by conveyed stimulations from stimulated points of the already known nerve network through the prostate. If this assumption were correct, the strength of the responses would be largest at the NVB. In this study, we have experienced that the amplitude size of the responses at the typical

Table 1. Patient data

Median age (y)	69.5 (IQR 67.0-71.3)
No. clinical stage	
T1c	8
T2a	4
No. biopsy Gleason score	
3 + 3	0
3 + 4	11
4 + 3	1
4 + 4, 4 + 5, 5 + 5	0
Median preoperative PSA (ng/mL)	7.3 (IQR 5.8-8.0)
Median excised prostate weight (g)	44.0 (IQR 38.5-50.0)

IQR, interquartile range; PSA, prostate-specific antigen.

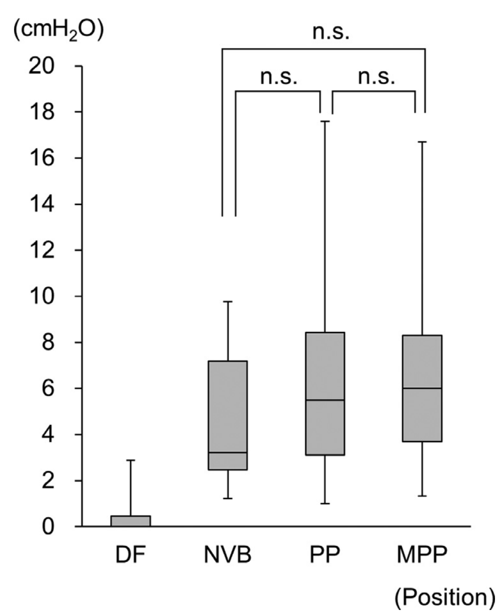

Figure 3. Median amplitude of pressure responses. The median amplitude of pressure responses at the PP, MPP and NVB was represented by box-and-whisker plot. MPP, medial side of the prostate pedicle; N.s., not significant; NVB, neuro vascular bundle; PP, prostate pedicle.

NVB stimulations was not necessarily stronger than those at the other stimulation points. We thus consider that nerve fibers at the posterior of the prostate also contribute to erectile function.

When interpreting the results of the present study, several limitations must be considered. First, the major limitation of our study was the small number of patients investigated. However, the same results were observed in all 12 patients, with electrostimulation at the posterior area of the prostate increasing cavernosal pressure. Although a limited number of patients were investigated, we consider the uniformity of the findings as sufficient indication that the posterior nerve fibers may substantially contribute to erectile functions. Future studies assessing improved outcomes of postoperative erectile function in patients with preservation of posterior nerve fibers are warranted. Second, the present study uses changes in the middle urethral pressure via balloon catheter to assess increases in the cavernosal pressure instead of inserting a needle directly into the cavernous body of the penis. Although the urethral pressure is not strictly the same as the cavernosal pressure, the intraurethral catheter method was employed because we found that the pressures in both of these compartments were correlated in all previous cases and that more stable responses can be obtained while reducing invasiveness.

CONCLUSION

Our results demonstrated that many nerve fibers responsible for erectile functions are contained in the PP and MPP as well as at the typical NVB. These findings indicate that we should take care not to cut into the tissues just outside of the DF during posterior dissection of the prostate. Similar to the preservation of the nerve network at the posterolateral, lateral, and ventral sides of the prostate, the preservation of the posterior tissues as much as possible, including the PP and MPP just outside of the DF, can contribute to optimal recovery of erectile functions after surgery.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.05.048.

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EDITORIAL COMMENT

This is a helpful study by Kaiho, Y. et al. that, during robotic prostatectomy, assessed the functional distribution of the "periprostatic nerve network" responsible for erectile function. Using electrical stimulation through a bipolar electrode (which produces a very localized electrical filed), points along the traditional neurovascular bundle and the posterior surface of the prostate were tested for their ability to induce a pressure rise within the penis. The findings suggest the nerves responsible for erectile function may span further along the posterior prostate surface than the area routinely preserved during typical nerve sparing.

Similar to what CaverMap facilitated in exploring the functional anatomy of the cavernous nerve during the era of open prostatectomy, this study provides insight into the neuroanatomy relevant to the robotic age.[1] In particular, the current study provides functional anatomic information from the cranial viewpoint that is central to the usual robotic base-to-apex dissection. This knowledge complements that gained in the open surgery era, where the apex-to-base approach was generally used, and the neurovascular bundles were viewed from an anterior perspective.

Overall, the findings in this study can be applied during nerve sparing to potentially aid the preservation of more neural tissue that facilitates erection. The utility of this approach to intraoperative stimulation as a guide for nerve sparing is unclear, but may be of limited benefit if history repeats itself. While the CaverMap was intended for this, it fell from favor due to a limited usefulness in identifying what tissues to preserve, as well as a poor ability to predict postoperative recovery of erectile function based upon intraoperative testing.[1]

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