Erectile function following unilateral cavernosal nerve replacement

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Introduction: *With nerve-sparing techniques, patients undergoing a radical prostatectomy may avoid the morbidity of erectile dysfunction. Certain patients who are not candidates for nerve-sparing procedures may be eligible for nerve interposition grafts. While bilateral cavernosal nerve grafting after radical prostatectomy has shown efficacy, the effect of unilateral nerve grafting following prostatectomy remains unclear. We evaluate a large group of patients who underwent a unilateral cavernosal nerve replacement.*

Methods: *Forty patients underwent unilateral nerve sparing surgery with concomitant contralateral cavernosal nerve replacement. Patients were selected for this procedure based upon preoperative nomogram risk assessment, endorectal MRI evidence of extra capsular disease (ECE) or intraoperative histology demonstrating margin positivity. Age, demographic data, Gleason score, clinical and pathologic stage and pre and post operative IIEF data was collected and prospectively analyzed.*

Results: *Median follow-up was 19 months. Median change in IIEF scores was 7.5. Twenty-one of 29 patients (72%) report being able to penetrate after prostatectomy. Sixteen of those 21 (76%) continue to require PDE-5 inhibitors to facilitate penetration. Four of the 6 patients (67%) who were unable to have intercourse following cavernosal nerve replacement received adjuvant hormonal and/or radiation therapy.*

Twenty-eight patients (97%) reported numbness at the graft harvest site. One patient experienced a graft site infection. Two of 29 (7%) patients reported pain at the harvest site.

Conclusion: *Unilateral sural nerve grafting is a feasible and well-tolerated approach for patients who must undergo wide resection of a NVB. While men do show a decrease in their IIEF score, 76% are able to achieve penetration following surgery. The majority of men continue to require PDE-5 inhibitors to facilitate intercourse.*

Key Words: prostate cancer, nerve graft

Introduction

Approximately 218,890 new cases of prostate cancer will be diagnosed in the United States in 2007[1] with the majority of these patients having organ-confined disease. Patients with organ-confined disease have a 10-year disease free survival between 70%-85%.[2] The treatment goal for these patients is to optimize cancer specific survival while minimizing the impact on continence and potency. Technical advancements in radical prostatectomy have resulted in 50%-80%[3,4] potency preservation rates when both neurovascular bundles (NVB) are spared. When only one NVB is spared, potency rates decrease to 30%-50%.[5,6]

Loss of potency results in a clear reduction in quality of life.[7] Even though there are options to treat sexual dysfunction in the postoperative patient, maintaining spontaneous erections remains the goal. Recently, there has been renewed interest in cavernosal nerve grafting to increase potency after one or both neurovascular bundles have been resected at the time of radical prostatectomy.[8,9]

Methods

Forty patients underwent open radical retropubic prostatectomy with unilateral nerve cavernosal nerve replacement by a single surgeon (JMC) from January 2003 to December 2006. All patients underwent a unilateral neurovascular bundle resection based on

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clinical exam, high Gleason score or preoperative imaging studies suggestive of invasive local disease. Inclusion criteria for cavernosal nerve replacement included informed consent, adequate preoperative potency based on IIEF (> 20), and planned unilateral resection of NVB. Exclusion criteria included peripheral neuropathy and preoperative use of phosphodiesterase inhibitors.

All patients underwent a radical prostatectomy with a standard nerve-sparing technique on the contralateral side. On the side of neurovascular bundle resection, the main cavernous nerve fiber was identified and marked at either end prior to resection. While loupe magnification was employed to identify dissection planes, the Cavermap system was not used. After removal of the prostate, the urethral anastomotic sutures were placed. Sural nerve grafts were used for all interposition grafts after being harvested by a dedicated neuro-otologist or head and neck surgeon. The graft was performed in the standard fashion as described by Kim et al[10] and was sewn in place under loupe visualization. Once the graft was in place, the urethral anastomosis was completed taking great care to ensure that the nerve was not disturbed.

Postoperative penile rehabilitation included: PDE-5 inhibitor three times weekly for 3 months followed by institution of intracavernosal injection therapy on postoperative day #90 in the absence of a functional erection.

Age, demographic data, Gleason score, and clinical and pathologic stage were collected and prospectively analyzed. Pre and post operative erectile function assessment was assayed using the validated IIEF-25 questionnaire. In addition a series of questions regarding a patient's erectile function and his sural graft site, Figure 1 were used. A physician who was not associated with the patients administered these surveys.

Erectile function

1. Have you been able to achieve penetration/intercourse after your prostate cancer surgery?
   Yes or No
2. Did you use Viagra, Cialis, or Levitra on a routine basis after surgery for rehabilitation of erections?
   Yes or No
3. Do you use Viagra, Cialis, or Levitra now to help with erections?
   Yes or No
   If so (circle): Never Sometimes Most of the time All the time
4. Do you use any other erectile aids such as penile injection therapy, vacuum pump devices, or intraurethral therapy?
   Yes or No

Nerve graft

1. Have you experienced any problems from your surgical site on your leg?
   Yes or No
2. Do you have numbness at your leg site?
   Yes or No
   If so, does this bother you? Yes or No
3. Do you have pain at your leg site? Yes or No
   If so, would you describe it as (circle): Mild Moderate Severe
   If so, do you take any pain medication for this problem? Yes or No
4. Have you experienced any other problems from your leg site?
   If so, what?

Figure 1. Supplemental questionnaire

TABLE 1. **Demographic data**

Number of patients	29
Mean age (range)	54.5 (44-69)
Follow-up (months)	
Median	28.7
Range	10-50.7
Mean pre-operative PSA (ng/ml) (range)	7.20 (1.69-25)
Gleason score 6	3
Gleason score 7	18
Gleason score 8-10	8
Pathologic stage	
pT2	18
pT3a	6
pT3b	5

Results

Full demographic and interview data was available for 29 of 40 patients (72.5%), Table 1. Median follow-up was 28.7 months (range 10-50.7 months). The median age at RRP was 54 with a median preoperative PSA of 6.5.

Median pre and post operative IIEF scores were 25 and 15 respectively. Median change in IIEF scores was 9 (range 1-23), Table 2. Twenty-one of 29 patients (72%) reported being able to penetrate after prostatectomy. Sixteen of those 21 (76%) continued to require PDE-5 inhibitors to facilitate penetration while five men required no adjuvant medication. Six of the eight patients (75%) who were unable to have intercourse following cavernosal nerve replacement received adjuvant hormonal and/or radiation therapy for advanced disease.

Twenty-eight patients (97%) reported numbness at the graft harvest site. Three (10%) described the numbness as bothersome. One patient experienced a graft site infection. Two of 29 (7%) patients reported pain at the harvest site.

TABLE 2. **Erectile function after RRP**

Median preoperative IIEF	25
Median postoperative IIEF	15
Median change in IIEF	9
Postoperative intercourse	21/29 (72%)
Current use of PDE-5	16/21 (76%)

Discussion

Radical retropubic prostatectomy is a gold standard therapy for localized prostate cancer with a 10 year PSA free recurrence rate of 73%. Technical advances in the past decade have enabled the urologist to perform this procedure with less impact upon patients' quality of life. Erectile dysfunction, however, remains a common concern for most patients. Potency outcomes after surgery are directly related to the quality and number of neurovascular bundles that are preserved. Resection of the neurovascular bundle during radical prostatectomy may be indicated in patients with high-grade disease or advanced local disease to provide optimal oncologic control.[11]

The use of peripheral nerves for grafting is an established surgical procedure in otolaryngology, orthopedics and neurosurgery. Grafting provides a physical conduit that allows regenerating nerve fibers to grow.[12] The use of a sural interposition graft has been extensively studied with brachial plexus, facial nerve and peripheral nerve injuries. In contrast to the central nervous system, the peripheral nervous system is capable of regeneration following injury or loss of continuity. Peripheral nerve regeneration rates average 1 mm/day and are probably slower in middle-aged men and those with associated comorbidities. Successful regeneration involves the extension of axonal growth cones through the interposed graft segment and then down the distal in-situ segment.[13] The predicted time to recovery of function is greater than 1 year. Erectile function after preservation of both NVB's has been shown to range from 50%-80%[6] while unilateral preservation reduces this rate to approximately 30%-50%.[14] The successful use of bilateral interposition grafts after non-nerve sparing RRP has also supported the use of nerve grafting principles.[15] Recent studies detailing experiences with unilateral nerve grafting with either genitofemoral[16] or sural[8] techniques have shown varying rates of success from 32% to 63% with approximately 2 year follow-up.

This study demonstrates penetration rates of 72%. This data correlates well with recent work by Sim et al[8] who found a 63.2% rate of erections suitable for intercourse in men who underwent a unilateral sural nerve graft. Patients in our series were slightly younger (54.5 years) than in series reported by Sim (57.2 years). The primary difference in surgical technique between the two series was the initial use of the Cavermap Surgical Aid System™ early in Sim's series to facilitate identification of anatomic landmarks. They conclude, and our study confirms that use of such mapping system is not required.

In our study, 72%t of men who underwent unilateral interposition graft with contralateral nerve sparing procedure were able to achieve intercourse at a median follow up of 28.7 months. The majority of these men were dependent on oral medications to assist them. Of the eight patients who reported no successful intercourse after radical prostatectomy, six underwent adjuvant therapy for advanced local disease. While the majority of men reported numbness at their graft harvest site, only three patients described this as bothersome and only two described this as painful. One patient reported a graft site infection as a complication from this procedure.

This study has several limitations. Foremost, because this is not a randomized protocol one cannot distinguish between enhanced sexual function secondary to nerve replacement versus improved outcome due to patient selection. Patients who elect to proceed with nerve replacement surgery are clearly highly motivated to pursue postoperative rehabilitation. That factor alone may account for the improved outcome. In a matched series of patients, however, the authors note penetration rates of 38% following unilateral nerve sparing techniques without contralateral nerve replacement (unpublished data). The program for rehabilitation of sexual function is identical between the two groups (PDE-5 inhibitor three times weekly for 3 months followed by institution of intracavernosal injection therapy on postoperative day #90 in the absence of a functional erection).

Further in regards to patient selection, the median age of men undergoing sural nerve replacement in this series was 54 years. Age has been shown to be an important factor in the maintenance of post prostatectomy potency.[17] While age is a factor in the success of potency sparing surgery, it is unlikely that this factor alone accounts for a potency rates that nearly double the published rates of 30%-50% rate for unilateral nerve sparing cases.[14]

Conclusion

Unilateral sural nerve grafting is a feasible and well-tolerated approach for patients who must undergo wide resection of a NVB. While men do show a decrease in their IIEF score, 76% are able to achieve penetration following surgery. The majority of men continue to require PDE-5 inhibitors to facilitate intercourse. □

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