Nerve Graft in Association with Radical Prostatectomy

Description

Nerve grafting to replace cavernous nerves resected at the time of radical prostatectomy is proposed to reduce the risk of erectile dysfunction after this surgery. The sural nerve is most commonly used in grafting.

Background

Erectile dysfunction is a common problem after radical prostatectomy. In particular, spontaneous erections are usually absent in patients whose extent of prostate cancer requires bilateral resection of the neurovascular bundles as part of the radical prostatectomy procedure. A variety of noninvasive treatments are available, including vacuum constriction devices and intracavernosal injection therapy. However, spontaneous erectile activity is preferred by patients. Studies have reported results from bilateral nerve grafts; there are also reports of unilateral grafts when only one neurovascular bundle has been resected.

There has been interest in sural nerve grafting to replace cavernous nerves resected at the time of prostatectomy. The sural nerve is considered expendable and has been used extensively in other nerve grafting procedures, such as brachial plexus and peripheral nerve injuries. As applied to prostatectomy, a portion of the sural nerve is harvested from one leg and then anastomosed to the divided ends of the cavernous nerve. Reports are also being published using other nerves, such as the genitofemoral nerve.

Regulatory Status

As sural nerve transplant is a procedure, it is not subject to FDA regulation.

Related Policies

None
Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Unilateral or bilateral nerve graft is considered not medically necessary in patients who have undergone resection of one or both neurovascular bundles as part of a radical prostatectomy.

Rationale

The first randomized controlled trial (RCT) that evaluated nerve grafting was published in 2009 by Davis and colleagues. (1) Eligibility criteria included age 65 or younger, normal self-report baseline erectile functions, and scheduled for a unilateral nerve-sparing radical prostatectomy with preservation of one neurovascular bundle. All patients had the other neurovascular bundle removed, and patients were randomly assigned to receive or not receive sural nerve grafting after its removal. The primary outcome was potency 2 years post-surgery, defined as the ability to have intercourse with or without erectile dysfunction medication. The investigators estimated that the control group would have a 40% potency rate and powered the study to detect an absolute difference of 20% between groups. All patients received the same early erectile dysfunction therapy including medication and mechanical devices. A sample size of 200 was originally planned to provide 80% power. However, after 107 patients were randomly assigned, a pre-planned interim analysis of evaluable patients found similar rates of potency in the two groups; the Data Monitoring Committee estimated that there was less than a 5% chance that there would be a significant difference between groups with additional recruitment and the trial was stopped early. When data collection ended, endpoint data were available for 66 patients who had either achieved potency or had been followed up for 2 years without potency. Potency was achieved in 32 of 45 (71%) sural nerve graft patients and 14 of 21 (67%) control patients (p=0.78). The authors concluded that unilateral sural nerve graft did not result in an absolute improvement of 20% in the rate of potency but that a smaller effect cannot be ruled out. A limitation of the study was that it was non-blinded, which could have impacted self-report of potency.

Other than the Davis et al. study, the published literature consists of case series described below.

A recent case series reviewed the records of 131 men who had unilateral nerve grafts after radical prostatectomy with unilateral neurovascular bundle resection. (2) Men who had prior radiation or hormonal treatment were excluded. Another eligibility criterion was satisfactory erections presurgery as assessed by a 5-point scale (1=full erections; 2=diminished erections, but routinely sufficient for sexual intercourse; 3=partial erections occasionally satisfactory for intercourse; 4=partial erections unsatisfactory for intercourse; and 5=no erections). A total of 49 men received sural nerve grafts, 79 received genitofemoral nerve grafts and 3 received ilioinguinal nerve grafts. Recovery of erections was evaluated at each follow-up visit according to the 5-point scale (also called 5 levels). The median patient age was 58.7 years, and the median follow-up was 37 months. According to actuarial analysis, the 5-year probability of recovering erections of level 3 or better was 46%. The probability of recovering erections of at least level 2 or level 1 was 34% and 12%, respectively.
In 2007, Namiki and colleagues published a series in Japan with 3-year follow-up. (3) A total of 113 patients were evaluated: 19 patients with unilateral nerve sparing plus sural nerve graft, 60 patients with unilateral nerve sparing but no grafting, and 34 patients with bilateral nerve-sparing surgery. Sexual function was assessed with validated questionnaires, and at 2 years there was no difference between the nerve-grafted and the bilateral nerve-sparing patients with regard to sexual function scores. At 3 years, 25% and 28% of patients in the nerve-grafted and bilateral nerve-sparing groups, respectively, considered their sexual function as fair or good. Urinary function returned to baseline in the nerve-grafted and bilateral nerve-sparing groups at 6 months and in the unilateral nerve-sparing group at 12 months. Differences in sexual function were present at baseline with the nerve-grafted and bilateral nerve-sparing patients reporting higher baseline function than the unilateral nerve-sparing group.

Sim et al. reported on 2-year results in 41 patients who received unilateral sural nerve grafts following radical prostatectomy when 1 neurovascular bundle was resected. (4) In this series, recovery of erectile function was reported for 63% of patients (based on 24 of 38 patients). This study also reported on erectile function on another group of patients who had unilateral resection at the same institution but without a nerve graft. In this group, which was older and was not matched on key characteristics to the group who received a nerve graft, the erectile function was 26.5% (13 of 49).

A study by Secin and colleagues had 5-year follow-up. (5) The authors reported results on 44 consecutive patients who underwent bilateral nerve grafting from 1999 to 2004 at Memorial Sloan-Kettering Cancer Center. The overall 5-year recovery of erectile function was 34%, and the rate of consistent function was 11%. None of a number of variables (e.g., age, type of nerve [sural, genitofemoral, ilioinguinal], comorbidities) was significantly associated with recovery of postoperative erectile function.

A 2001 study, by Kim et al., included men with clinically localized, but high-volume prostate cancer such that bilateral resection of the neurovascular bundles was considered necessary. (6) Before surgery, all men reported spontaneous erection. The results were compared to a group of 12 men who were potent preoperatively and had undergone prostatectomy with bilateral nerve resection but who declined nerve graft placement. Of the 23 men undergoing nerve grafting, 6 (26%) had spontaneous, medically unassisted erection sufficient for sexual intercourse. An additional 6 men (26%) reported 40% to 60% spontaneous erection that was insufficient for intercourse; 4 of these patients were able to have intercourse using sildenafil. Therefore, a total of 10 of the 23 patients were able to have intercourse, either spontaneously or with pharmacologic therapy. A total of 11 men had no clinical response even with the use of sildenafil. Not unexpectedly, all outcomes were significantly better compared to the control group. Side effects of the sural nerve donor site, which included incisional pain and a sensory deficit along the lateral aspect of the foot, were considered tolerable. The authors noted improvement 8 to 12 months postoperatively and accelerated improvement at 12 to 18 months postoperatively.
Ongoing Clinical Trials

Nerve Grafting With an Allograft During Radical Prostatectomy - Extended Follow-up in a Prospective Randomized Trial (NCT01770340) (7): This single-blind study includes 60 patients with prostate cancer. Patients have been randomized to receive radical prostatectomy with or without implantation of an allogenic nerve graft. The primary outcome is erectile function and follow-up is at least 24 months post-surgery. The expected date of final data collection is January 2014.

Practice Guidelines and Position Statements

The 2013 (V.4) National Comprehensive Care Network (NCCN) prostate cancer guidelines states that replacement of resected nerves has not been shown to be beneficial for recovery of erectile function after radical prostatectomy. (8)

Summary

Nerve-grafting, most commonly using the sural nerve, at the time of radical prostatectomy has been proposed to reduce the risk of postoperative erectile dysfunction. Only one randomized controlled trial that evaluated sural nerve grafting with radical prostatectomy has been published, and this study did not find that unilateral sural nerve grafting was associated with a statistically significant improvement in potency rates 2 years post-surgery. Due to the negative findings of this study, and the lack of other controlled studies evaluating unilateral or bilateral nerve grafting, the technique is considered not medically necessary.

Medicare National Coverage

No national coverage determination.

References


Policy History

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Keywords

Genitofemoral Nerve Graft, Prostatectomy
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 14, 2014 and is effective April 15, 2014.

Signature on File
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