Nerve Graft to Restore Erectile Function During Radical Prostatectomy

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Instructions for Use

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Application

This Medical Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Indiana	None
Kentucky	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for Kentucky Only)
Louisiana	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for Louisiana Only)
New Jersey	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for New Jersey Only)
New Mexico	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for New Mexico Only)
Ohio	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for Ohio Only)
Pennsylvania	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for Pennsylvania Only)
Tennessee	Nerve Graft to Restore Erectile Function During Radical Prostatectomy (for Tennessee Only)

Coverage Rationale

Autologous (e.g., sural) or allogenic nerve grafts to restore erectile function during or after radical prostatectomy are unproven and not medically necessary due to insufficient evidence of efficacy.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
55899	Unlisted procedure, male genital system
64999	Unlisted procedure, nervous system

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Description of Services

Erectile dysfunction (ED) is a common problem after radical prostatectomy (RP). In particular, spontaneous erections are absent in those who have bilateral resection of the neurovascular bundles as part of the RP procedure for treating localized prostate cancer. A technique called nerve-sparing surgery has been developed to prevent damage to these nerves; however, this technique is not possible for some people.

Nerve grafting to replace resected cavernous nerves during radical retropubic prostatectomy (RRP) has been proposed as a technique to increase the likelihood of restoring spontaneous erectile function (EF). During the procedure, a donor nerve (e.g., sural nerve, genitofemoral nerve) is harvested from the person and joined to the distal and proximal ends of the resected cavernous nerve. Grafting may be performed on one or both resected cavernous nerves. The sural nerve (a nerve traveling along the short saphenous vein in the lower leg) is the most common donor nerve used in the nerve grafting procedure during RP. The nerve is considered expendable and has been used commonly in other nerve grafting procedures for repairing injured peripheral nerves. During the sural nerve grafting (SNG) procedure, a portion of the nerve is harvested from one leg of the individual and grafted to the resected cavernous nerve.

Advocates of nerve grafting believe that nerves should be preserved whenever compatible with complete resection of cancer, but that when the cavernous nerve must be resected or is damaged severely, graft replacement should be a consideration (Kim et al., 2001; Scardino et al., 2001). While the decision to spare or resect the neurovascular bundles is based on the surgeon's preference, it is influenced by clinical stage, prostate-specific antigen level, and transrectal ultrasound/biopsy results (Kim et al., 2001).

Clinical Evidence

There is insufficient quality scientific evidence in the clinical literature demonstrating that using nerve grafting results in improved outcomes for ED following RP. Single-arm and non-randomized observational studies suggest a possible benefit, but one available randomized trial was ended early due to lack of benefit at the intermediate analysis. This suggests that the findings of the non-randomized studies may have been biased. Some of these non-randomized studies did in fact show baseline differences in participants undergoing nerve grafting compared to those not undergoing this procedure.

Harke et al. (2023) conducted a case series to investigate the safety and feasibility of spider silk grafting for erectile nerve reconstruction for individuals undergoing robotic radical prostatectomy (RARP). The major-ampullate-dragline from Nephila edulis was used for spider silk nerve reconstruction (SSNR). After removal of the prostate with either unilateral or bilateral nerve-sparing, the spider silk was laid out on the site of the neurovascular bundles. Data analysis included inflammatory markers and patient-reported outcomes. Six participants underwent RARP with SSNR. In 50% of the cases, only a unilateral nerve-sparing (UNS) was performed, bilateral nerve-sparing could be performed in three people. The placement of the spider silk conduit was uneventful, contact of the spider silk with the surrounding tissue was mostly sufficient for a stable connection with the proximal and distal ends of the dissected bundles. Inflammatory markers peaked until postoperative day one but stabilized until discharge without any need for antibiotic treatment throughout the hospital stay. One participant was readmitted due to a urinary tract infection. Three people reported erections sufficient for penetration after three months with a continuous improvement of EF both after bilateral and UNS with SSNR up to the last follow-up after 18 months. The authors concluded this analysis of the first RARP with SSNR, a simple intraoperative handling without major complications was demonstrated. While the series provides evidence that SSNR is safe and feasible, a prospective randomized trial with long-term follow-up is needed to identify further improvement in postoperative EF due to the spider silk-directed nerve regeneration. Given the nonrandomized design of this study and the retrospective nature of data collection and analysis, one cannot rule out residual confounding factors that could influence the results. Further research is needed to determine the clinical relevance of these findings.

Shauly et al. (2019) conducted a systematic review of recent articles and identified 19 articles/studies addressing relatively new interventions for ED. The review documented evidence supporting the use of two microsurgical treatments for ED - namely microvascular arterial bypass penile revascularization surgery and cavernous nerve graft reconstruction. For cavernous nerve graft reconstruction, the authors identified six publications, but they all seem limited by the lack of a comparison group. Although the authors indicated that their analysis served to organize the most up-to-date data in treating ED and showed promise, they concluded that many of the studies lacked a large enough study population to make material claims and further clinical evidence is required.

Reece et al. (2019) performed a retrospective review of a single-center experience of nerve grafting in a case series of seventeen men who had ED following RP surgery. Microsurgical bilateral end-to-side nerve grafts from a selective fascicular neurotomy of the femoral nerve to the penile corpora cavernosa was performed. The median age at nerve

grafting was 64 years [interquartile range (IQR) 60-66 years]. Median time between nerve- and non-nerve sparing RP and nerve grafting was 2.4 (IQR 2.1-3.1) and 2.2 (IQR 1.7-5.1) years, respectively. Median follow-up was 18 (IQR 15-24) months. At 12 months after nerve grafting, 71% (95% CI 44-90%) of people had EF recovery sufficient for satisfactory sexual intercourse, and 94% (95% CI 71-99%) and 82% (95% CI 57-96%) had clinically significant improvements in sexual function and reduced bother, respectively. There were two minor wound infections. The authors indicated this provided confirmatory evidence that end-to-side nerve grafting surgery restored EF and improved sexual quality of life in, respectively, 71% and 94% of men with ED following RP. The authors recognized that the limitations include the retrospective study design and concluded that larger studies to determine EF recovery rates utilizing end-to-side nerve grafting to restore EF in men with post-RP ED are advised to confirm its efficacy and feasibility. The findings are limited by the lack of a comparison group.

Souza Trindade and colleagues (2017) conducted a long-term case series study on 10 participants at 6, 12, 18, and 36 months postoperatively for those who had surgery involving bridging the femoral nerve to the dorsal nerve of the penis and the inner part of the corpus cavernosum with sural nerve grafts nerve grafts and end-to-side neurographies after having undergone a RP at least two years previously. Four participants also underwent radiotherapy after RP. All participants reported satisfactory sexual activity prior to RP. The surgery involved bridging of the femoral nerve to the dorsal nerve of the penis and the inner part of the corpus cavernosum with sural nerve grafts and end-to-side neurographies. Participants were evaluated using the IIEF questionnaire and pharmaco-penile Doppler ultrasonography (PPDU) pre-operatively and at 6, 12, and 18 months post-operatively, and using a Clinical Evolution of Erectile Function (CEEF) questionnaire, administered after 36 months. The IIEF scores showed improvements regarding ED, satisfaction with intercourse and general satisfaction. Evaluation of PPDU velocities did not reveal any difference between the right and left sides or among the different time-points. The introduction of nerve grafts neither caused fibrosis of the corpus cavernosum, nor reduced penile vascular flow; CEEF results showed that sexual intercourse began after a mean of 13.7 months with frequency of sexual intercourse varying from once-daily to once-monthly. The authors concluded that a total of 60% of individuals were able to achieve full penetration, on average, 13 months after re-innervation surgery. Those who previously submitted to radiotherapy had slower return of erectile function. The authors concluded that penile re-innervation surgery is a viable technique, with effective results, and could offer a new therapeutic option for ED after RP. This study was limited by the small number of cases (n = 10) and the lack of a comparison group.

Kung et al. (2015) performed a retrospective study on 38 consecutive participants who underwent immediate unilateral or bilateral nerve reconstruction after open prostatectomy. Additionally, 53 control participants who underwent unilateral, bilateral, or non-nerve-sparing open prostatectomy without nerve grafting were reviewed. Outcomes included rates of urinary continence, erections sufficient for sexual intercourse, and the ability to have spontaneous erections. Analysis was performed by stratifying participants by D'Amico score and laterality of nerve involvement. There was no significant benefit for individuals who had unilateral nerve grafting (UNG) versus UNS prostatectomy. Participants with bilateral nerve-sparing (BNS) demonstrated superior functional outcomes compared to those with bilateral non–nerve-sparing, whereas those with bilateral nerve-grafting displayed a trend toward functional improvement. With increasing D'Amico score, there was a trend toward worsening urinary continence and EF regardless of nerve-grafting status. The authors concluded that immediate nerve grafting for reconstruction of the prostatic plexus after RP may be most valuable for improving postoperative morbidity in those requiring bilateral neurovascular bundle resections. Currently, the benefit of nerve grafting is limited by the inability to accurately isolate the putative nerves, which mediate EF and urinary continence. Further investigation is needed to improve the potential of bilateral nerve grafting after non–nerve-sparing prostatectomy. Limitations to this study include the small sample size, the subjective nature of the postoperative outcomes, and the lack of randomization to intervention groups.

Siddiqui et al. (2014) examined the long-term outcome of SNG during RRP performed by a single surgeon. Sixty-six participants with clinically localized prostate cancer and preoperative International Index of Erectile Function (IIEF) score > 20 who underwent RRP were included. Neurovascular bundle excision was performed if the risk of side-specific extra-capsular extension was > 25% on Ohori's nomogram. SNG was harvested by a plastic surgeon, contemporaneously as the urologic surgeon was performing RRP. IIEF questionnaire was used pre- and post-operatively and at follow-up (3 years). Recovery of potency was defined as post-operative IIEF-EF domain score > 22. There were 43 (65%) unilateral SNGs and 23 (35%) bilateral SNGs. The mean preoperative IIEF score was 23.4 + 1.6. Long term assessment reflected 19 participants (28.8%) had IIEF scores > 22. The IIEF-EF scores for those who had unilateral SNG and bilateral SNG were 12.9 + 4.9 and 14.8 + 5.3, respectively. The authors concluded that SNG can potentially improve EF recovery for potent men with higher stage prostate cancer undergoing RP; and that the contemporaneous, multidisciplinary approach provides a good quality graft while expediting the procedure without interrupting the workflow. However, the evidence is insufficient to conclude that this surgical technique is equivalent to BNS prostatectomy or that long-term outcomes are improved by nerve grafting. The findings are limited by lack of relevant comparison group.

Davis et al. (2009) evaluated whether UNS RP plus SNG would result in 50% relative improvement in potency at 2 years compared to UNS RP alone. The plan was to enroll 200 participants from October 2001–May 2006 in a RCT from a single academic center. After 107 participants were randomized in a 3:2 ratio (66 SNG, 41 controls), a protocol-planned interim analysis was performed which reflected potency rates of 18 of 41 (44%) in the SNG group and 10 of 23 (43%) in the control group. Based upon slower-than-estimated accrual (8 per month planned vs. 2 per month actual) and a < 5% posterior probability that the groups would show a difference, the Data Monitoring Committee recommended early termination of the trial. Using data gathered from the 107 participants, the authors concluded that in this single-institution randomized study, unilateral SNG did not result in an increased potency rate at 2 years compared to UNS RP alone based upon a threshold significance level of at least a 20% (absolute) improvement. Secondary endpoints also did not show an improvement in time to potency or urinary function at 1 year. Based upon the power of this study, a smaller benefit could not be excluded. The authors believed that future study designs should anticipate inconsistent compliance with penile rehabilitation and 20-30% patient attrition.

Sugimoto et al. (2009) evaluated 24 patients who underwent UNS with contralateral cavernous nerve-grafting or bilateral nerve-grafting and 64 patients who underwent prostatectomy without nerve-sparing procedure. Patients in the nerve-grafting group who recovered potency demonstrated higher sexual function scores compared with those without nerve-sparing procedure. However, the majority of these patients were not satisfied with their sexual function. The findings are limited by lack of randomization, which could have introduced a bias in the findings.

Kuwata et al. (2007) prospectively investigated health-related quality of life, including sexual function, in 66 patients who underwent nerve grafting during a RP in comparison with those who underwent a non-nerve-sparing RP (22 patients had nerve-grafting procedures, 44 underwent non-nerve-sparing and non-nerve-grafting procedures). The observation periods ranged from 12-46 months (median: 29 months). For individuals who had nerve-sparing graft procedures (bilateral or unilateral), the sexual function score was significantly better than in the non-nerve-sparing/non-nerve-grafting patients. The sexual bother score, however, was more serious for the patients who underwent nerve-grafting surgery than for the non-nerve-sparing/non-nerve-grafting patients. The findings are limited by lack of randomization, which could have introduced a bias in the findings.

Saito et al. (2007) evaluated 64 patients who underwent a RP and intraoperative electrophysiological confirmation of cavernous nerve preservation. Twelve patients underwent a unilateral SNG for the resected neurovascular bundle. Twenty-one and 31 patients underwent BNS and UNS surgery without a nerve graft, respectively. As the age of patients was significantly younger in the SNG group than in the other groups, age-matched analysis also was conducted. In the age-matched analysis, the postoperative sexual function (SXF) score of the SNG group showed an intermediate level of recovery between those of the BNS and UNS groups at 12 months and reached the same level as the score at 12 months of the BNS group at 18 months postoperatively. The difference in the SXF score between the SNG and UNS groups began to appear after 6 months postoperatively and increased steadily with time. However, the background factors, such as the baseline SXF score, the usage rate of phosphodiesterase 5 inhibitors, and the rate of comorbidities were different between the SNG and UNS groups.

A prospective observational study by Namiki et al. (2007) evaluated 113 patients undergoing RRP for the rate of recovery of urinary continence and sexual potency. Patients were classified into three groups according to the degree of nerve sparing: unilateral nerve preservation with contralateral SNG interposition, BNS, and UNS. The BNS group showed the fastest recovery, although by 24 months there were no significant differences observed between the BNS group and the UNS group with SNG. The BNS group reported a better sexual function score than the UNS group throughout the post-operative period. During the first year post-operatively, the BNS group and the UNS group with SNG had better urinary function results than the UNS group. The authors concluded that the nerve graft procedure may contribute to the recovery of urinary function as well as sexual function after RRP; these findings are limited by lack of randomization.

Clinical Practice Guidelines

American Urological Association (AUA)

The 2018 American Urological Association guideline on ED recommends six types of treatment that could be considered for ED. Three are medications, while the others are vacuum erection devices, penile prosthesis implantation, and penile arterial reconstruction. Treatments not recommended are venous surgery, low-intensity extracorporeal shock wave therapy, intracavernosal stem cell therapy, and platelet-rich plasma therapy (Burnett et al., 2018).

Guideline 11 specifically states men who desire preservation of EF after treatment for prostate cancer by RP or radiotherapy (RT) should be informed that early use of phosphodiesterase-5 inhibitors (PDE5i) post-treatment may not improve spontaneous, unassisted erectile function. (Moderate Recommendation; Evidence Level: Grade C).

National Comprehensive Cancer Network (NCCN)

According to the National Comprehensive Cancer Network (NCCN) prostate cancer guideline, recovery of EF following RP is related directly to the degree of preservation of the cavernous nerves, age at surgery, and preoperative erectile function. Improvement in urinary and sexual function has been reported with nerve-sparing techniques. Replacement of resected nerves with nerve grafts does not appear to be effective for patients undergoing wide resection of the neurovascular bundles (NCCN, 2022; updated 2024).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Sural nerve transplant is a procedure, and as such, is not regulated by the FDA.

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Policy History/Revision Information

Date	Summary of Changes
11/01/2024	**Supporting Information** • Updated *Description of Services*, *Clinical Evidence*, and *References* sections to reflect the most current information

Date	Summary of Changes
	• Archived previous policy version CS081.M

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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