NERVE GRAFT TO RESTORE ERECTILE FUNCTION DURING RADICAL PROSTATECTOMY

Guideline Number: MMG086.I **Effective Date**: September 1, 2019

Instructions for Use

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Related Policies

None

COVERAGE RATIONALE

Sural or other nerve grafts to restore erectile function during 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 guideline 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 the member specific benefit plan document 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 patients who have bilateral resection of the neurovascular bundles as part of the RP procedure for treatment of localized prostate cancer. A technique called nerve-sparing surgery has been developed to prevent damage to these nerves; however, this technique is not possible in some patients.

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 patient 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 patient 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

In a 2017 review of peer reviewed published literature on surgical techniques for managing post-prostatectomy ED, Castiglione et al. found that with the failure of penile rehabilitation and the lack of evidence for accessory pudendal artery preservation and nerve graft, nerve-sparing surgery and penile prostheses represent the only methods to date to permanently and definitively preserve EF after RP.

Kung et al. (2015) performed a retrospective study on 38 consecutive patients who underwent immediate unilateral or bilateral nerve reconstruction after open prostatectomy. Additionally, 53 control patients 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 ability to have spontaneous erections. Analysis was performed by stratifying patients by D'Amico score and laterality of nerve involvement. There was no significant benefit for patients who had unilateral nerve grafting (UNG) versus unilateral nerve-sparing (UNS) prostatectomy. Bilateral nerve-sparing (BNS) patients demonstrated superior functional outcomes compared with bilateral non–nerve-sparing patients, whereas bilateral nerve-grafting patients 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 patients 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 small sample size and the subjective nature of the postoperative outcomes.

Siddiqui et al. (2014) examined the long term outcome of SNG during RRP performed by a single surgeon. Sixty-six patients 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' nomogram. SNG was harvested by a plastic surgeon, contemporaneously as the urologic surgeon was performing RRP. IIEF questionnaire was used pre- and postoperatively and at follow-up (3 years). Recovery of potency was defined as postoperative IIEF-EF domain score >22. There were 43 (65%) unilateral SNG and 23 (35%) bilateral SNG. The mean preoperative IIEF score was 23.4+1.6. Long term assessment reflected 19 patients (28.8%) had IIEF score >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 work-flow. 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.

Davis et al. (2009) wanted to evaluate 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 patients from October 2001–May 2006 in a RCT from a single academic center. After 107 patients 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, early termination of the trial was recommended by the Data Monitoring Committee. 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.

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). 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.

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 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 3 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 postoperative period. During the first year postoperatively, 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; however these findings need to be validated in a RCT.

According to the National Comprehensive Care Network (NCCN) prostate cancer guideline, replacement of resected nerves with nerve grafts has not been shown to be beneficial for recovery of EF after RP (2019).

A clinical trial is recruiting participants in order to evaluate the use of the implantation of the allogenic nerve graft Avance® in patients undergoing non nerve-sparing RP. For more information, go to www.clinicaltrials.gov. (Accessed June 25, 2019)

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

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

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GUIDELINE HISTORY/REVISION INFORMATION

Date	Action/Description
09/01/2019	**Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information; no change to *Coverage Rationale* or *Applicable Codes* • Archived previous policy version MMG086.H

INSTRUCTIONS FOR USE

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Management Guideline is provided for informational purposes. It does not constitute medical advice.

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