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**PERSPECTIVE**

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**IMPROVING CANCER CONTROL AND RECOVERY OF POTENCY AFTER RADICAL PROSTATECTOMY: NERVE SPARING VERSUS NERVE RESECTION WITH GRAFTING**

The primary goal of radical prostatectomy is to ensure complete removal of the cancer with preservation of urinary and sexual function. The surgical dilemma involves whether it is safe to preserve the so-called neurovascular bundle (NVB) if there is a risk of extracapsular extension (ECE) and positive surgical margins (+SM).

The authors are to be commended for providing a timely, succinct and thorough review of the recently published data on the utility and safety of nerve grafting and in the process have identified three main concerns that remain unanswered:

First, is the lack of high-level evidence supporting the technique and the tremendous variability in the results reported. Bilateral grafts have been reported to result in recovery of potency of between 34% (ref. 25) and 72% (ref. 26) compared to 0 in men undergoing bilateral NVB resection without grafting. Both series used the Cavermap nerve stimulator to mark the proximal NVB before resection, which may have improved results. The Cavermap has been shown in clinical and experimental studies to allow surgeons to more accurately detect the NVB (1, refs 13, 27 and 40). However, bilateral wide resection is rarely required and with recent evidence of a survival advantage to adjuvant radiotherapy for pathological T3 disease many of these men will be offered radiation, further minimizing the likelihood of recovery. Furthermore, with the stage migration to more organ-confined disease occurring in the prostate-specific antigen era, a patient requiring bilateral wide resection will become very rare indeed. Increasingly patients with high-risk features will only be offered surgery as part of multimodality trials, including postoperative therapies, which will have a dramatic impact on the likelihood of recovery of potency.

The series quoted report that between 58 and 64% of men recover after unilateral grafting carried out at open surgery, which does compare favourably to historical controls of unilateral wide resection of approximately 30%.<sup>1</sup> The efficacy of unilateral grafts cannot be determined because of substantial confounders, including the lack of a standardized technique, the use of different conduits including sural or genitofemoral nerves, the reliance on historical controls with more contemporary grafted patients having access to phosphodiesterase inhibitors and aggressive rehabilitation. Genitofemoral nerves are smaller in calibre than sural and might be, as a very recent study suggests, both inferior in efficacy and associated with significant sensory deficit.<sup>2</sup>

However, proof of efficacy can only be determined by randomized trials, which are unlikely to be undertaken because of difficulties in blinding patients and clinicians, sample size considerations, limited access to the Cavermap nerve stimulator, adjusting for the Hawthorne effect and the changes in surgical technique.

Currently our unit offers nerve grafting only on an ethics approved protocol with strict selection criteria and makes use of the Cavermap to identify the proximal NVB before resection with exclusive use of the sural nerve resulting in a +SM rate of only 4%.

Second, is the anatomy of the cavernous nerves in humans. The authors discuss studies by Walsh and others (refs 19 and 20), but do not include elegant studies by Takenaka *et al.* on fresh cadavers, which have shown that the NVBs, covered by the lateral pelvic fascia, are located more than 20–30 mm below and more than 20 mm distal to the bladder–prostate junction.<sup>3</sup> The erectile nerves tended to be located outside the NVB at the dorsolateral margin of the prostate. These authors concluded that ‘In contrast to general clinical opinion, the NVB appears to supply few pelvic splanchnic nerve components at the bladder prostate junction with caudal pelvic splanchnic branches reaching the dorsolateral prostate more than 20 mm lower’. These authors suggest that the proximal placement of the nerve graft, therefore, could have a dramatic effect on the likelihood of success particularly if the Cavermap is not used to map and mark the proximal NVB. The authors acknowledge that the absence of the Cavermap in some series reviewed in this manuscript may account for the wide variation in outcomes reported as the proximal end of the graft may not be placed in the optimal position.

Tewari *et al.* recently carried out similar studies of 10 fresh cadavers and described a trizonal neural architecture with considerable variability.<sup>4</sup> Tewari *et al.* described a proximal neurovascular plate located 5 mm (3–10 mm) lateral to the seminal vesicles, 3 mm (2–7 mm) thick, 7 mm (5–25 mm) wide and 9 mm (4–30 mm) long. It was within 6 mm (4–15 mm) of the bladder neck, 5 mm (2–7 mm) of the endopelvic fascia and overlapped 5 mm (0–7 mm) of the proximal prostate. There was a predominant NVB, which varied in shape and size from the proximal to distal end, was thickest at the base and most variable near the apex. In 66% of cases, there was a medial extension behind the prostate, which converged medially at the apex in 33% cases. Accessory neural pathways were noted within the layers of levator fascia and/or lateral pelvic fascia on the anterolateral aspect and on the posterior aspect of the prostate underscoring the variability of neural anatomy.

Clearly, these studies suggest that the variability in neural anatomy is significant and that results of grafting will be dramatically affected by the placement of the graft in optimal position. Our limited understanding of the anatomy should not be a deterrent to grafting but rather a stimulus to improve our understanding of the anatomy and thereby improve our techniques of partial NVB preservation or wide resection of the NVB with grafting if appropriate.

Finally, the necessity of wide excision of the NVB at the time of radical prostatectomy requires consideration. Mancuso *et al.* importantly discuss the role of partial NVB preservation. As recent anatomical studies show that the NVB is located up to 20 mm away from the base of the prostate and on average 5 mm away in other areas. They and others suggest that perhaps it is possible to carry out partial NVB preservation, ensuring clear margins and complete removal of the tumour, but with preservation of enough NVB to allow recovery of potency.

The importance of achieving –SM is not to be understated and it is pleasing that the authors have devoted some discussion to this topic. The authors conclude that in patients with ECE, nerve sparing leads to a higher proportion of positive surgical margins than wide local excision (refs 32 and 36–8). Positive margins, in general, lead to a fourfold increased risk of biochemical progression with many of these patients undergoing salvage treatments. It is well worth remembering that nomograms predict up to 80% of patients will achieve long-term cure by surgery alone of pathological T3 disease (ECE) if negative margins are achieved. However, this cure rate falls to 36% or less if positive margins occur.

The decision to carry out nerve sparing therefore is critical and is generally based on preoperative clinicopathological variables. However, intraoperative palpation of the prostate with open surgery has been shown to have significant positive predictive value in studies by both Walsh (ref. 30) and Brendler and coworkers.<sup>5</sup> The absence of haptic feedback with laparoscopic-assisted or robotic-assisted laparoscopic prostatectomy is a concern in this regard, where decisions are made on the safety of nerve sparing without knowledge as to induration in the region of the NVB.

Very few studies have reported on the results of partial NVB preservation. The paper by Rabbani *et al.*, I believe, provides the best information on the recovery of potency with varying degrees of preservation of the NVB and is elegant as it pre-dates the sildenafil era.<sup>2</sup> This large single surgeon series of Scardino from Baylor suggests that the detriment in recovery of erectile function is only 9% if partial nerve sparing is carried out.

In this series 76% of the young men recovered with bilateral nerve sparing, 67% with unilateral partial preservation, but only 30% with complete unilateral resection. Bilateral wide resection of the NVB rendered all men completely impotent.

Comments attributed to Walsh in the discussion section of the paper need to be interpreted with caution as heavily screened populations in the USA are at less risk of ECE, allowing Walsh to suggest that wide resection of the NVB is rarely required. Recent series reported in the robotic-assisted laparoscopic experience from the USA suggest that ECE is found in only 2–18% of patients, but when present +SM occur in 30–55%, suggesting that decision-making on safety of NVB preservation at robotic surgery needs to be further refined.<sup>6</sup> Australia and New Zealand have far less screened populations with less stage migration and therefore

a higher percentage of patients who are potentially amenable to nerve grafting. Furthermore, the fact that a procedure is uncommonly required does not mean that it should not be offered if there is a potential benefit with low morbidity.

In conclusion, the authors suggest that although the results of bilateral grafts are encouraging, they are seldom required and that unilateral grafts have not yet been shown to be useful. I would suggest that if bilateral grafts work then unilateral should, providing a trial was designed with optimal technique and sufficient power to show a difference. The morbidity of sural nerve grafts is low, but new technologies will likely render them obsolete with the use of alternative autologous or heterologous conduits.

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