

Review

Nerve-sparing radical retropubic prostatectomy: techniques and clinical considerations

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There are essentially two ways to accomplish nerve preservation during radical retropubic prostatectomy: the 'apical approach' described by Walsh and the so-called 'lateral approach', a simplified method where the dissection is initially conducted on the portion of the bundles that courses posterolateral to the prostate. Do the different techniques differ in the ability to preserve potency and in the positive surgical margins rate? No previous study has addressed this question. Above all, the preoperative and intraoperative indications to spare or not the nerves remain a matter of debate. The present review is an attempt to elucidate these questions in light of the current literature.

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Anatomical location of the neurovascular bundles

A precise knowledge of the neurovascular anatomy of the prostate is an essential prerequisite for a nerve-sparing (NS) approach to radical retropubic prostatectomy. This has been excellently refined in cadaveric studies by Walsh and co-workers.^{1,2}

The neurovascular bundles (NVB) that course posterolateral to the prostate consist of a complex structure related to the vascularization of the outer prostatic portion and to the innervation of the prostate, urethra and corpora cavernosa. Small arterial branches originating from the inferior vesical artery and venous vessels draining in the homonymous vein constitute the vascular portion of the bundles. They run in the lateral pelvic fascia, medially to the cavernosal nerve branches (*vide infra*) to terminate as capsular vessels that pierce the

prostatic fascia. These vessels are important when performing an NS radical retropubic prostatectomy (RRP) as they provide the landmark for the identification of the nerves.

The caudal portion of the pelvic plexus, located at the tip of the seminal vesicles, emanates autonomic fibres, which form a dense network with the described vessels.^{3,4} Some of them perforate the prostatic capsule to enter the substance of the prostatic gland. These branches are inevitably sacrificed during an NS approach, but it is believed that they do not contribute significantly to erectile function. The majority of nerve fibres, known as the cavernous branches, travel in a direct route from the pelvic plexus towards the posterolateral base of the prostate, gradually coalescing from a group of fibres approximately 12 mm wide to a more organized bundle approximately 6 mm wide at the level of the prostate. At this point, they lie just underneath the lateral pelvic fascia, between the levator fascia and the prostatic fascia (a fibrous layer in direct continuity with the true prostatic capsule). At the level of the membranous urethra, they are located at the 3 o'clock and 9 o'clock position, just beneath the striated sphincter that at this point surrounds both the urethra and the prostatic apex.

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Techniques of NS surgery during RRP

Two main surgical approaches to an NSRRP have been described.⁵ In the so-called 'anatomical technique', first reported by Walsh,^{2,6,7} the nerves dissection is initiated at the apical level with primary isolation of the urethra. Ruckle and Zincke⁸ have proposed an alternative technique where the neurovascular bundles are primarily dissected off the lateral prostate and only subsequently is the urethra transected. Several variants of this lateral approach to the neurovascular bundles have been subsequently described.⁹⁻¹¹

The apical approach to the NVB (the 'Walsh technique')⁷

There are a number of key steps in this technique that, if overlooked, may jeopardize the success of nerve preservation. For each of them, PC Walsh has provided useful tips to avoid inadvertent nerve injury during surgery. These are summarized below:

1. After division of the dorsal vein complex, the proximal vein edges on the anterior surface of the prostate need to be sutured in order to avoid back bleeding. This should be accomplished with a running V-shaped suture rather than trying to tie together the edges towards the midline. The latter manoeuvre may displace medially the bundles towards the anterior prostate, making their accurate dissection more difficult.
2. A critical point where the bundles may be damaged is during the transection of the urethra and the surrounding striated sphincter musculature. As the neurovascular bundle when approaching the prostatic apex is located underneath the sphincter and can be fixated into a medial position by an apical vessel, care should be used to transect only the lateral edges of the sphincter at the urethral level, refraining from any dissection underneath the prostatic apex.
3. In order to avoid excessive traction while releasing the bundles from the lateral prostatic surface, after the urethra has been transected the catheter should be removed and the dissection carried out while the prostate is rolled from side to side.
4. By releasing the superficial layer of the lateral pelvic fascia, the prostate becomes more mobile and the neurovascular bundles move laterally. This manoeuvre is best accomplished by lifting up the prostatic fascia with a right angle clamp starting at the bladder neck and proceeding down to the apex. At this point, a groove will appear on the posterolateral edge of the prostate as a landmark for the neurovascular bundle which is located just laterally to it. Following the groove down to the apex will enable the identification of the bundles at the level of the transected urethra: only at this point, can the dissection be completed at the apex and carried out posteriorly to develop the prostatic-rectal plane without damaging the nerves.
5. The bundles can now be released completely from the prostate with gentle spreading of a right angle from the apex up to the midportion of the prostate. Some vessels that pierce the prostate at this level may prevent the release of the bundle and need to be

divided with small hemoclips. Avoidance of unipolar electrocoagulation is of paramount importance for the maintenance of the integrity of the nerves.

6. The division of a small arterial vessel running from the neurovascular bundle, over the seminal vesicle to supply the prostatic base, usually enables the bundles to be completely freed from the prostate.
7. The last critical point for a successful NS technique is represented by the dissection of the seminal vesicles. As the midportion of the pelvic plexus is anatomically located at the tip of the seminal vesicles, the dissection of these small organs must be carried out very carefully, particularly in the lateral aspect, where small arterial branches are often encountered and need to be clipped close to the seminal vesicles.

The lateral approach to the NVB

The Ruckle and Zincke⁸ technique This technique represents an alternative and simplified anatomical approach in which the dissection of the neurovascular bundles off the prostate precedes the apical dissection and the urethral transection. Briefly, after blunt perforation of the lateral prostatic fascia bilaterally, the dorsal vein complex is transected in between a double ligation with the creation of an oval defect in the dorsal prostatic fascia.¹² A vertical incision in the prostatic fascia is then conducted from one of the two lateral sides of the defect (for example, the left) down to just above the left neurovascular bundle. From that point, the incision is extended superiorly towards the bladder and inferiorly towards the urethra parallel to the neurovascular bundle. Overall the incision, if carried out in the left side, will appear as an upside down T to the operator positioned on the left side of the patient. By placing the index finger at the confluence of the incisions in the prostatic fascia, the left neurovascular bundle is swept laterally from the prostate. A posterior prostatic plane is then created by advancing the finger between the two layers of the Denonvillier fascia: the anterior layer, attached to the posterior prostate, and the posterior one in contact with the rectum. The finger is further advanced until it reaches the lateral prostatic fascia of the contralateral right side. The fascia is then perforated and spread with a right angle clamp medially to the right neurovascular bundle. This manoeuvre enables the right bundle to be freed from the prostate.

The Scardino technique^{13,14} In this technique, following the transection of the dorsal complex, the lateral pelvic fascia is incised medial to the neurovascular bundle on the anterolateral prostatic portion and the bundles are gently swept laterally from the prostate. A lateral retraction of the bundle allows the Denonvillier fascia to be exposed. An incision is made on the posterior Denonvillier fascia that covers the prerectal fat. Care must be taken to preserve Denonvillier's fascia over the posterior prostate in order to reduce the risk of positive surgical margins (PSM).

The Klein et al⁹ variant technique The authors describe their NS technique as a modification of the initial

dissection of the perirectal lateral pelvic fascia reported by Stephenson *et al*¹⁵ in a non-NS surgical approach of RRP. In a way conceptually similar to that of Ruckle and Zincke⁸ and Scardino,^{13,14} the incision of the lateral pelvic fascia along the longitudinal axis of the prostate begins at a level well medial to the neurovascular bundles. The bundles are then swept inferiorly and laterally from the prostate and then sharply dissected free from the prostate from apex to base. When the bundles have been completely freed on both sides, the plane between the posterior prostate and the anterior rectum is developed with blunt dissection rotating the prostate from side to side. Only at this point are the dorsal vein and the urethra divided.

Do the different NS techniques differ in outcomes?

The surgeon considering an NSRRP must balance the need for complete eradication of local tumour with the preservation of sexual function. A successful NS technique should combine a high probability of potency recovery with a low PSM rate, particularly at the apex and the posterolateral prostate. Extensive literature has demonstrated that PSM adversely affect recurrence-free survival outcome after surgery.¹⁶⁻¹⁹ A PSM is defined by the majority of authors as the extension of the tumour to the inked surface of the resected specimen and is considered an indicator of incomplete excision of the neoplasm.^{20,21}

As the cavernosal nerves cannot always be visualized on the dorsolateral prostate surface, Walsh⁷ advises their identification at the prostatourethral junction after dissecting the apex of the prostate. On the contrary, the supporters of the lateral approach to the bundles contend that identifying the nerves at the apex is more difficult.⁸ Are these different approaches equally safe in terms of cancer control?

Ruckle and Zincke⁸ compared 104 consecutive patients who had undergone the original Walsh NS RRP before 1991 with 123 consecutive patients who had an NS procedure according to their modified technique after 1991. The PSM rate (32% in the Walsh technique *vs* 37% in the Ruckle and Zincke technique) did not significantly differ in the two groups. In a similar comparative study, Klein *et al*⁹ reported a reduction in PSM from 33.3% employing the Walsh technique to 15.5% when their modified lateral approach to the bundles was used. However, these retrospective analyses are biased by potential confounders such as stage migration, improvement in preoperative selection criteria and surgical expertise.

As far as sexual preservation is concerned, no study as yet has compared the degree of potency recovery among the different reported NS techniques. Outstanding postoperative potency rates varying from 86 to 62% have been reported employing the Walsh NS technique, but these seem to be confined only in centres of excellence.^{22,23} The success rate of the procedure drops to 44% in a large retrospective survey of nonspecialists²⁴ and falls to 21% in a single institutional prospective series assessing preoperative and postoperative outcomes with validated questionnaires.²⁵

Several factors may account for these discrepancies. Firstly, age and preoperative sexual functioning have been recognized as independent predictors of postoperative recovery of erectile function.²⁶ The chances of potency recovery decrease with the increase of age at time of the operation. The excellent results in the series of Walsh refer mainly to patients younger than 65 y.²⁷ Noh *et al*²⁸ reported that all patients younger than 50 y in his series regained postoperative sexual function compared with only 38% older than 70 y. Similarly, patients with some degree of erectile dysfunction prior to the procedure are more likely to develop severe erectile dysfunction postoperatively.²⁹ Another key factor is the timing for potency recovery. At 3 months postoperatively, only 38% of patients in the Walsh series were able to perform unassisted sexual intercourse, whereas potency had been regained by 86% at 18 months.³⁰ Whether the patient decides or not to undertake early postoperative pharmacological prophylaxis may have an additional impact on the subsequent recovery of erectile function.³¹⁻³³ Monolateral NS negatively affects potency recovery.³⁴ At least a 25% reduction in success rate is expected if only one neurovascular bundle can be spared at the time of surgery.²⁶

Finally, poor outcomes of an NSRRP may simply be the result of a suboptimal performance of the surgical technique. Recently, Walsh *et al*³⁰ reviewed the videotapes of 62 of his own NSRRP. Patient's reported potency rates were correlated with four specific steps of the procedure deemed to be crucial for a correct nerve preservation, namely, V-shaped oversewing of the back bleeders from the proximal dorsal vein on the anterior surface of the prostate, maintenance of a collar of striated sphincter lateral to the urethra while placing the sutures, division of the posterior striated sphincter at its midpoint between the apex and the urethral stump and achievement of excellent hemostasis at the end of the case. Notably, in all eight cases who failed to regain potency at 18 months, the technique was judged blindly as less than optimal for all the four steps described above.

Given the complex series of variables that can interfere with the success of a sexual sparing RRP, it has to be concluded that, out of a randomized prospective fashion, a comparison of potency outcomes for the different techniques of NSRRP may be an impossible task. No such study is at the moment available in the literature.

Indications for sparing or not sparing the neurovascular bundles

Preoperative indications

The majority of authors agrees that the ideal candidate for an NSRRP should be fully potent preoperatively and have an organ-confined cancer, that is, a clinical T1/T2a and T2b disease.²⁰ As the neurovascular bundles lie outside the capsule and fascia of the prostate, cancer control is not compromised by an NS procedure when the tumour is organ confined.

T1a and T1b are ideal for NS as they rarely invade the NVB.³⁵ T1c tumours have been reported to have a PSM rate varying from 0 to 59%,³⁶ so eligibility for an NS should be judged according to PSA and Gleason score.

Table 1 Preoperative and intraoperative selection criteria for not performing an NS procedure and the reported positive surgical margins rate

	Sofer <i>et al</i> ⁵⁸	Walsh ⁵⁹	Alsikafi and Brendler ⁴⁴	Graefen <i>et al</i> ⁴⁷	Scardino and Kim ⁵¹	Shah <i>et al</i> ⁶⁰
Preoperative selection criteria						
Clinical stage >T2	+	+	+	+	+	+
PSA >10 ng/ml	+					
GS=7			+			
GS>7	+			+		
GS≤6 if >50% tumour in biopsy ^a						+
GS=7 if >30% tumour in biopsy ^a						+
GS≥8–10 if >10% tumour in biopsy ^a						+
Partin tables		+			+	
Site of >50% tumour on biopsy ^a			+			
Site of perineural invasion ^a		+/-	+			+
Intraoperative selection criteria						
Site of palpable tumour ^a			+			
Site of positive biopsy ^a				+		
Induration of the lateral pelvic fascia ^a		+			+	
Adherence of the NVB to the prostate ^a		+			+	
Positive surgical margins	24%	5%	11%	15.9%	5%	8%

^aThe NVB can be spared on the contralateral side.
GS = Gleason score.

T2a and T2b cancers with a contralateral negative biopsy are considered low-volume localized diseases with a high probability to be organ confined.³⁷ Low Gleason score³⁸ and PSA are preferable since high preoperative PSA and biopsy grade increase the risk of extracapsular extension and therefore of PSM.^{39,40} As shown in Table 1, a clinical T1 and T2 prostate cancer with a PSA below <10ng and a Gleason score ≤7 constitute the main eligibility criteria for an NS procedure in the majority of authors. A useful tool to predict the probability of extracapsular tumour extension on the basis of preoperative parameters is represented by the Partin Tables.⁴¹ Cheng *et al*⁴² found the combination of PSA value and the percentage of cancer in the biopsy specimen to accurately predict the risk for positive margins and propose a model based on these two variables to select the candidates for NSRRP. Tigrani *et al*⁴³ studied 108 patients who underwent RP and found the number of positive biopsies and not PSA level, Gleason score or primary grade to be the best predictor of margins status.

Others have advocated even more strict inclusion criteria. The neurovascular bundle located on the site of a positive biopsy that contains more than 50% of tumour or perineural invasion or a Gleason 7 or higher tumour should be removed according to Alsikafi and Brendler.⁴⁴

Several authors have adopted the practice of sparing the nerve only on the site of a negative biopsy.^{45–48} By doing so, Huland *et al*⁴⁸ found a 0% incidence of PSM on the NS site while 27% of patients had disease in the removed bundle. Similarly, Park *et al*⁴⁵ found a 32% rate of extracapsular extension on the site of positive biopsy vs only 7% when the biopsy was negative. The site-specific removal of the neurovascular bundle resulted in a potential reduction of PSM in 50% of patients with extracapsular extension. In the series of Graefen *et al*,⁴⁷ the excision of the neurovascular bundle on the side of a positive biopsy excluded approximately 30% of patients from an NSRP unnecessarily, while the overall positive

margin rate was 15.9%. The utility of using such strict selection criteria is also questioned by the observation that 78% of patients with unilateral positive biopsies have bilateral tumour involvement at the examination of the entire specimen.³⁷

Walsh⁴⁹ states that the site of a positive biopsy or of a palpable tumour or the presence of perineural invasion represents strict criteria upon which the decision to excise a neurovascular bundle should be based. A previous study showed that only 17% of patients with perineural invasion had a PSM at the level of the neurovascular bundle.⁵⁰ Rather, a subjective intraoperative judgment is the most accurate indicator of the necessity to sacrifice the neurovascular bundle.⁷

Intraoperative indications

Walsh⁷ recommends to proceed to secondary excision of the NVBs (which should always be spared in the first instance), in the presence of one of the following intraoperative findings:

1. induration in the lateral pelvic fascia
2. adherence of the NVB to the prostate while it is being released
3. inadequate tissue covering the posterolateral surface of the prostate once the prostate has being removed.

Other authors employ the same criteria as intraoperative indicators of wider dissection.⁵¹ Alsikafi and Brendler⁴⁴ advocate wide excision of the neurovascular bundle(s) any time a tumour is palpable on one or both sides intraoperatively, particularly when at the apex. They describe the technique of transecting the anterior urethra 3 mm distal to the apex at all times.⁴⁴

Some authors have addressed the question of whether obtaining a frozen section of the apical soft tissue during an NSRRP may reduce the incidence of PSM at the prostatic apex, a site often involved in prostate cancer.⁵²

Shah *et al*⁵³ observed that the routine use of biopsy frozen section of apical soft tissue was responsible for achieving a disease-free status in only 2% of their patients. Other authors,⁵⁴ questioning the accuracy of preoperative assessment of the tumour extent by digital rectal examination⁵⁵ and a subjective intraoperative assessment of extracapsular extension,⁵⁶ decided to spare the bundles after obtaining intraoperative frozen sections in patients with prostate cancer at high risk of extracapsular extension. They reported a PSM rate of 26% and estimated that the frozen sections enabled a 15% reduction of PSM. However, tumour was identified in only 20% of specimens, confirming the finding of previous studies where most patients with positive intraoperative frozen sections did not have detectable tumour in the removed NVB.⁵⁷

Table 1 lists the indications criteria adopted in some high-volume institutions to decide whether or not to spare the neurovascular bundle(s). The PSM rates should not be taken as an absolute indicator of the validity of the reported criteria since they may largely be influenced by the surgical ability.

Does NS surgery affect the risk of PSM?

Since the surgical boundaries are reduced by performing an NS procedure, this may result in a higher rate of PSM, particularly in the posterolateral prostate. The region of the neurovascular bundle has been shown as the most common site of capsular penetration.^{15,61} Using the NS procedure, Catalona and Bigg⁶² reported that all patients with extracapsular extension in the region of the neurovascular bundle had PSM.

In spite of these premises, it is a fact that, irrespective of the widespread use of an NS approach, the overall rate of PSM has continuously declined over the last two decades.²⁰ A shift in the prostate cancer population towards an intracapsular disease, together with refinements in surgical technique⁶³ and improvement in surgical expertise,⁶⁴ is the most likely explanation. In the presence of these confounds, it becomes difficult to interpret the potential negative impact of NS procedures.

A few studies have addressed the question of whether NSRRP patients may have an increased risk of PSM. Scardino's group^{65,66} documented a further decrease in PSM from 19% in 1989 to 8% in 1993 in spite of the introduction of their lateral approach to the neurovascular bundle. Similarly, earlier reports failed to demonstrate a statistically significant difference in the rate of positive margins between NS and non-NSRRP.⁶⁷⁻⁶⁹ Overall PSM rates were 24% in NS patients and 31% in NNS ones in the series of Sofer *et al*.⁵⁸ The two groups of patients were also equally distributed as regards the incidence of posterolateral margins. Even after adjusting the patients for the major potential prognostic factors the NS status seemed to affect cancer control. In the light of these results, several authors nowadays believe that in appropriately selected patients, the NS approach does not compromise cancer control and that no more than 7% of PSM can be attributed to nerve preservation.^{70,71} In the most recent series by Walsh⁵⁹ of 500 consecutive patients, in which the NVB was widely excised only on one side in 13% of cases, the overall PSM rate was 5%.

Recently, a large multicentric retrospective review of 9035 RPs performed in the last 20 years found the overall PSM rate falling from 40% between 1982 and 1986 to 10% between 1997 and 2002. However, the PSM rate in the pT3 disease population slightly increased between 1997 and 2002, implying that the decrease in surgical margins rates is most likely due to stage migration rather than major improvement in surgical technique.⁷² Since patients, particularly the pT3 group, were not stratified according to nerve preservation, the potential negative impact of the NS technique remains to be elucidated.

When present, an extensive capsular perforation has been reported to occur in the region of the neurovascular bundles in 87% of cases, resulting in 57% of PSM.⁶⁵ Negative surgical margins were achieved in 58% of cases after wide excision of the bundles, compared with a 45% rate when both bundles were left intact in a series of 107 patients with posterolateral extensive capsular perforation. Long-term follow-up showed a sustained improvement in disease-free survival for the negative margins patients.⁷³ Park *et al*⁴⁵ introduced the concept of the ratio between the PSM rate and the extracapsular extension (ECE) rate to assess the benefit of excising the neurovascular bundle. He found that in series employing more liberal indications for NS the PSM/ECE ratio was higher⁷¹ than in those using more conservative NS approaches (68 *vs* 50).^{37,74}

A PSM may also be the result of cutting through inside the glandular area of the prostate.⁷⁵ An NS procedure is expected to carry a higher risk of these 'intraprostatic surgical margins'. Based on the histological review of a large series of NSRRP patients, inadvertent capsular incision during surgery had occurred in no more 2.3% of cases.⁷⁶ Even if these figures may be too optimistic, literature data have shown intraprostatic surgical margins have little or no effect on oncological outcome.^{66,77}

These studies, taken together, suggest that NSRRP nowadays does not seem to have a significant impact on prostate cancer control as the majority of patients elected for surgery have an organ-confined disease. Continuous improvement in diagnostic criteria will probably help to better identify those patients with extracapsular extension for whom the preservation of bundles may translate into PSM.

The challenge of the future

The technique of sparing the erigentes nerves during radical prostatectomy was described more than 20 y ago. The operation is currently routinely performed worldwide, but excellent results, particularly for potency preservation, seem to be confined in few centres of excellence. The improvement in cancer control demonstrated by a slight but continuous reduction of the PSM rate over the years has not been accompanied by a similar increase in potency preservation. There is even the suspicion that the better oncological results may simply reflect a stage migration and not an amelioration of the surgical technique.

Will NSRRP outcomes improve in the future? Or will the challenge of improving the results be taken over by new surgical techniques? The first consistent series of NS laparoscopic radical prostatectomy have shown

outcomes comparable to open surgery so far.^{78,79} A comparative study of open and laparoscopic radical prostatectomy has shown overlapping results for PSM (7.3 vs 7.8%) and potency rates (65 vs 55%).⁸⁰ As yet we do not know if the laparoscopic technique has reached its zenith or whether it will continue to improve, perhaps with the assistance of the robot. It may be possible that what we have so far described as outcomes of the NSRRP will represent an unsurmountable bar for any sort of surgical approach. If this turns out to be the case, some may even dare to ponder whether the future of prostate cancer cure should be surgical at all.

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