

Different Nerve-Sparing Techniques during Radical Prostatectomy

Subjects: [Urology & Nephrology](#)

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Nerve-sparing technique during RP has a major impact to both oncological and functional outcomes of the procedure and various different techniques have been developed aiming to optimize its outcomes. Nerve-sparing techniques can be distinguished based on the fascial planes of dissection (intrafascial, interfascial or extrafascial), the direction of dissection (retrograde or antegrade), the timing of the neurovascular bundle dissection off the prostate (early vs. late release), the use of cautery, the application of traction and the number of the neurovascular bundles which are preserved.

prostate cancer

radical prostatectomy

nerve-sparing

techniques

1. Basic Principles of NS Techniques

NS techniques can be distinguished depending on the fascial planes which are dissected (intrafascial, interfascial or extrafascial), the direction used during dissection (antegrade, retrograde or a combination of two), the timing of the NVB release off the prostate (before or after manipulations on the prostatic vascular pedicles), the use of cautery (thermal or athermal), the application of traction (traction-free or non-traction-free techniques) and the number of the NVBs which are preserved (unilateral or bilateral NS). Transection, cautery, crush and traction are underlying mechanisms by which the cavernous nerves can be injured during manipulations, and many NS techniques have been developed in order to avoid one or more of them [\[1\]](#). Despite this rough categorization, several alternative NS techniques have been developed which cannot be integrated into one of the categories described above.

2. The Fascial Planes for NS

The prostate and the bladder are covered by a multilayer fascia called the endopelvic fascia, which is linked with both of them by collagen fibers. At the level of the prostate, the endopelvic fascia has an inner part overlying the prostate (prostatic fascia) and an outer part (Levator fascia or Lateral Pelvic Fascia). Posteriorly, the prostate and the seminal vesicles are covered by the Denonvilliers' fascia, which laterally merges with the endopelvic fascia. Finally, a layer of fibromuscular smooth muscle located between the prostatic glandular units and the periprostatic connective tissue, along with vessels and nerves, constitute the prostatic capsule [\[2\]](#). Based on the exact fascial plane of dissection, three different NS techniques can be described (**Figure 1**). In extrafascial NS, dissection is performed under the Denonvilliers' fascia, as evidenced by the presence of perirectal fat on the posterior aspect of

the dissection plane. In interfascial NS, the prostatic fascia is retained intact and dissection is performed within the plane between the prostatic fascia and the lateral pelvic fascia, which extends posteriorly as the plane between the prostatic fascia and the Denonvilliers' fascia. Although the original NS procedure described by Walsh was performed using the interfascial technique, the discovery of supplementary nerve fibers on the anterolateral surface of the prostate promoted the development of the intrafascial technique in an attempt to preserve them [3]. In intrafascial NS, dissection is performed within the plane between the prostatic capsule and the prostatic fascia. At the end of the intrafascial dissection, no additional tissue over the prostate is identified.

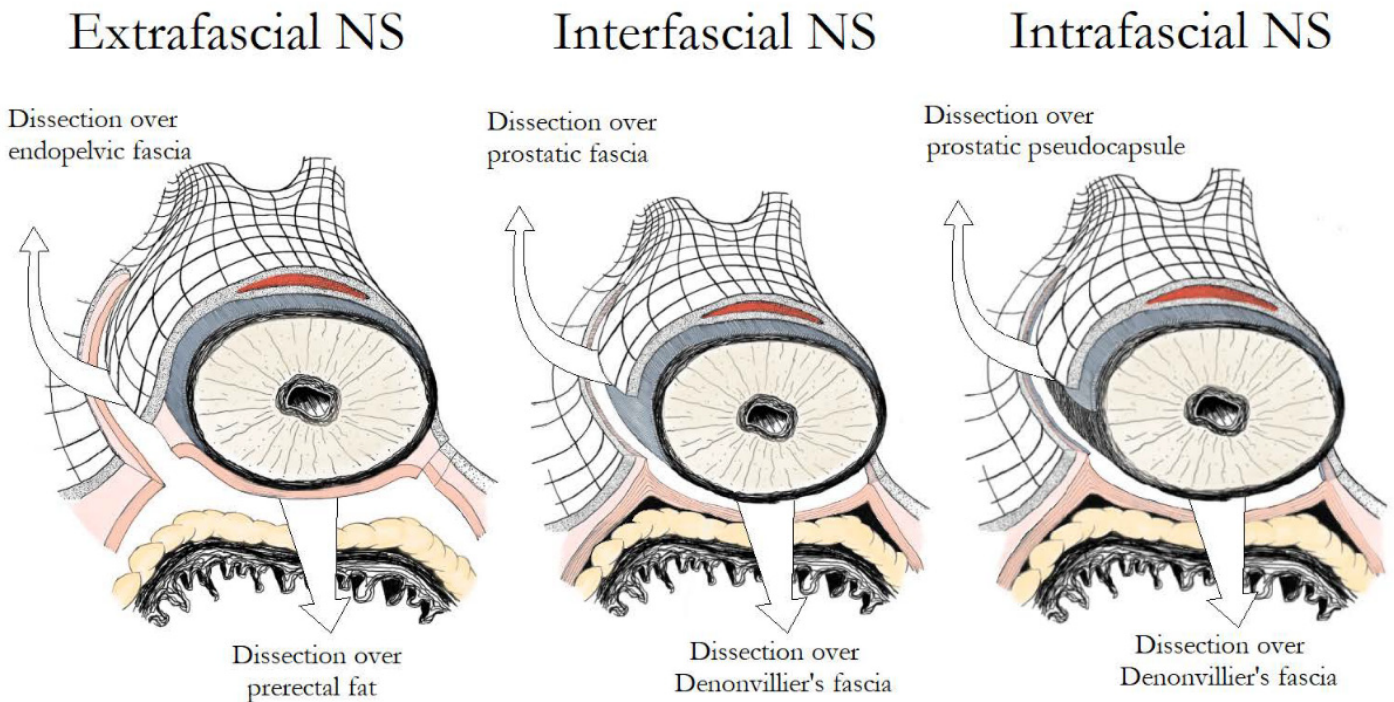


Figure 1. Main differences in fascial development between extrafascial, interfascial and intrafascial nerve-sparing.

2.1. Intrafascial vs. Interfascial NS

Several studies have examined the impact of different fascial planes of NS on the functional outcomes of RP. Khoder et al. conducted a prospective study, in which 430 patients were included, comparing open complete intrafascial with interfascial RP. They concluded that the intrafascial prostatectomy offers better functional results in comparison to the interfascial approach, without compromising the oncological results a year after the procedure [4]. In another study including 147 patients, Potdevin et al. compared the outcomes of intrafascial versus interfascial NS in robotic-assisted radical prostatectomy (RARP). The authors observed a higher potency rate and a shortened time of the return of continence following the intrafascial technique. Nevertheless, the positive surgical margin rates were higher in patients with pT3 disease in the intrafascial group [5]. Stolzenburg et al. compared the outcomes for interfascial and intrafascial NS endoscopic extraperitoneal RP, coming to the conclusion that the intrafascial technique is associated with significantly better potency in patients <55 years of age at 12 months and in patients 55–65 years of age at 6 and 12 months, with probably limited effect on the oncological outcomes. Moreover, the intrafascial technique was also associated with significantly improved continence rates at 3 and 6 months after

surgery as compared with the interfascial approach [3]. Although many studies report better outcomes following the intrafascial technique, the oncological safety of this procedure has been called into question. Curto et al. found a positive surgical margin rate of 30.7%, associated with the intrafascial approach, a rate much higher than that of other interfascial series [6]. In contrast, Wang et al. noted that the intrafascial NS, when cases are carefully selected, could offer an acceptable or, at least, equivalent positive surgical margin rate compared with the conventional interfascial approach [7]. In a recent meta-analysis, performed by Weng et al., the intrafascial technique has proven to be superior to the interfascial technique in terms of functional outcomes, likely due to lesser nerve damage. The research demonstrated better continence at 6 months and 36 months and better potency recovery at 6 months and 12 months postoperatively, associated with the intrafascial approach. Surprisingly, cancer control was also better with the intrafascial technique, possibly because patients in the interfascial group presented higher-risk cancer than patients in the intrafascial group [8]. The key steps of intrafascial NS are depicted in **Figure 2**.

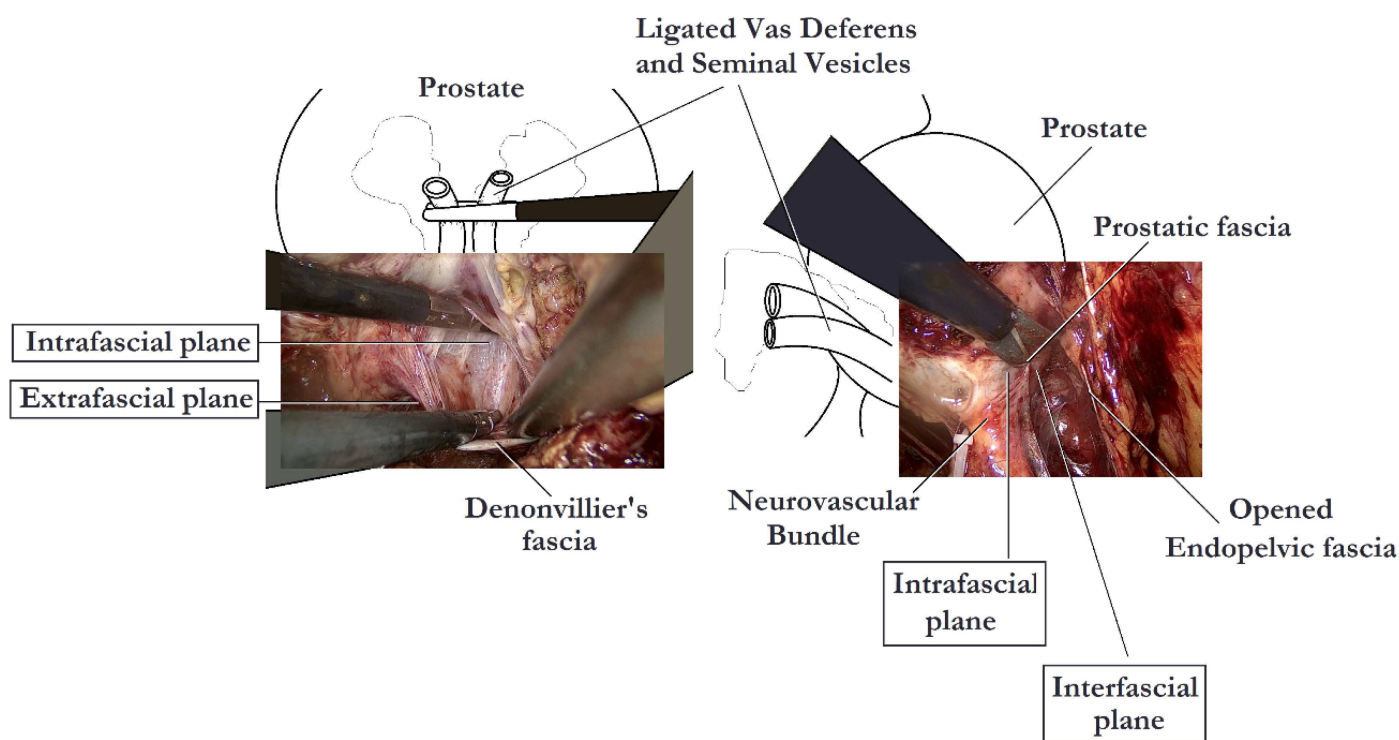


Figure 2. Nerve-sparing intrafascial laparoscopic radical prostatectomy.

2.2. Extrafascial vs. Non-Extrafascial (Intrafascial and Interfascial) NS

Shikanov et al. compared 110 cases of bilateral extrafascial NS versus 703 cases of interfascial NS. They observed significantly better sexual function in patients undergoing bilateral interfascial NS, while in lower-risk patients, bilateral interfascial NS did not result in significantly higher positive surgical margins rates [9]. Zhao et al. in a meta-analysis including 2096 patients from 7 eligible studies, compared the oncological and functional outcomes of intrafascial with non-intrafascial RP (including interfascial, extrafascial and no nerve-sparing approaches) in patients with low-risk localized prostate cancer. The meta-analysis demonstrated that the oncological outcomes were similar between the two groups, while the intrafascial approach was associated with

lower postoperative complication rates, higher continence rates at 3 months and higher potency rates at 6 and 12 months following surgery, as compared to the non-intrafascial approaches [10].

3. Different NS Grading Systems

Various alternative grading systems have been proposed to describe the different degrees of NS. The intrafascial plane corresponds to the maximal extent of NS, while the extrafascial plane corresponds to the minimal extent. Montorsi et al. divided NS into full, partial and minimal as matching intrafascial, interfascial and partial extrafascial dissections, respectively [11]. Tewari et al. proposed a new 4-degree stratification for the preservation of the neurovascular bundles, using the veins which are situated on the lateral aspect of the prostate as landmarks. According to them, grade 1 matches a complete intrafascial dissection and is a dissection between the periprostatic veins and the pseudocapsule of the prostate. Grade 2 matches an interfascial dissection and is a dissection performed just over the veins, while grade 3 dissection leaves more tissue over the veins and the prostate. Finally, grade 4 matches an extrafascial dissection [12]. Schatloff et al. proposed a 5-degree stratification for the definition of the dissection planes, using the “landmark artery” (LA), which runs on the lateral aspect of the prostate, as a reference point. The LA can be recognized, intraoperatively, in up to 73% of cases. A grade 5 dissection, during which the prostate and the NVBs can be separated without the need for sharp dissection, matches a maximal NS (complete intrafascial dissection) and is performed medially to the LA just outside the prostatic fascia. A grade 4 dissection is performed using sharp dissection in a plane between the LA and the prostatic pseudocapsule across the NVB, while in a grade 3 dissection, the plane of NS is created laterally to the LA, and thus the artery is clipped at the level of the prostate pedicle. Finally, for a grade 2 dissection, NS is performed several millimeters laterally to the artery, while for a grade 1 dissection, an extrafascial dissection is performed and the NVBs are not spared (Figure 1) [13]. A summary of the different grading systems is demonstrated in Table 1.

Table 1. Different nerve-sparing grading systems.

Nerve-Sparing Grading System	References	Anatomical Landmark	Number of Grades	Description of Different Grades
Fascial planes	Stolzenburg et al. [3]	Periprostatic fasciae	3	<ul style="list-style-type: none"> • Intrafascial • Interfascial • Extrafascial
Extent of nerve-sparing	Montorsi et al. [11]	Neurovascular bundles	3	<ul style="list-style-type: none"> • Full nerve-sparing (matches to an intrafascial dissection)

Nerve-Sparing Grading System	References	Anatomical Landmark	Number of Grades	Description of Different Grades
				<ul style="list-style-type: none"> • Partial nerve-sparing (matches to an interfascial dissection) • Minimal nerve-sparing (matches to a partial extrafascial dissection)
<p>4-degree approach for preservation of the neurovascular bundles</p>	<p>Tewari et al. [12]</p>	<p>The veins which are situated on the lateral aspect of the prostate</p>	<p>4</p>	<ul style="list-style-type: none"> • Grade 1 (matches to a complete intrafascial dissection) • Grade 2 (matches to an interfascial dissection) • Grade 3 • Grade 4 (matches to an extrafascial dissection)
<p>5-degree approach for the definition of the dissection planes</p>	<p>Schatloff et al. [13]</p>	<p>The “landmark artery” (LA), which runs on the lateral aspect of the prostate</p>	<p>5</p>	<ul style="list-style-type: none"> • Grade 1 (matches to an extrafascial dissection) • Grade 2 • Grade 3 • Grade 4 • Grade 5 (matches to a complete

3. The Direction of NS

Nerve-Sparing Grading System	References	Anatomical Landmark	Number of Grades	Description of Different Grades	Description
				intrafascial dissection)	tion. The last after and robotic from the

prostate, before controlling the posterior pedicle [1][14]. Patel et al. described their technique of early retrograde release of the NVBs during RARP in an athermal way with minimization of traction. In order to perform this approach, the LA must first be recognized in the lateral aspect of the prostate. A plane is developed between the LA and the prostate, which is continued posteriorly, and then the dissection proceeds in a retrograde way towards the base of the prostate (**Figure 3**). Prostatic pedicles are clipped last, resulting in a natural traction-free release of the NVBs off the prostate. Describing their results in 397 patients, they reported that 87.7% of patients with Sexual Health Inventory for Men (SHIM) >21, and 73% with SHIM between 17 and 21 preoperatively, were potent with or without the use of phosphodiesterase-5 inhibitors, after a 3-month follow-up [2][13][14].

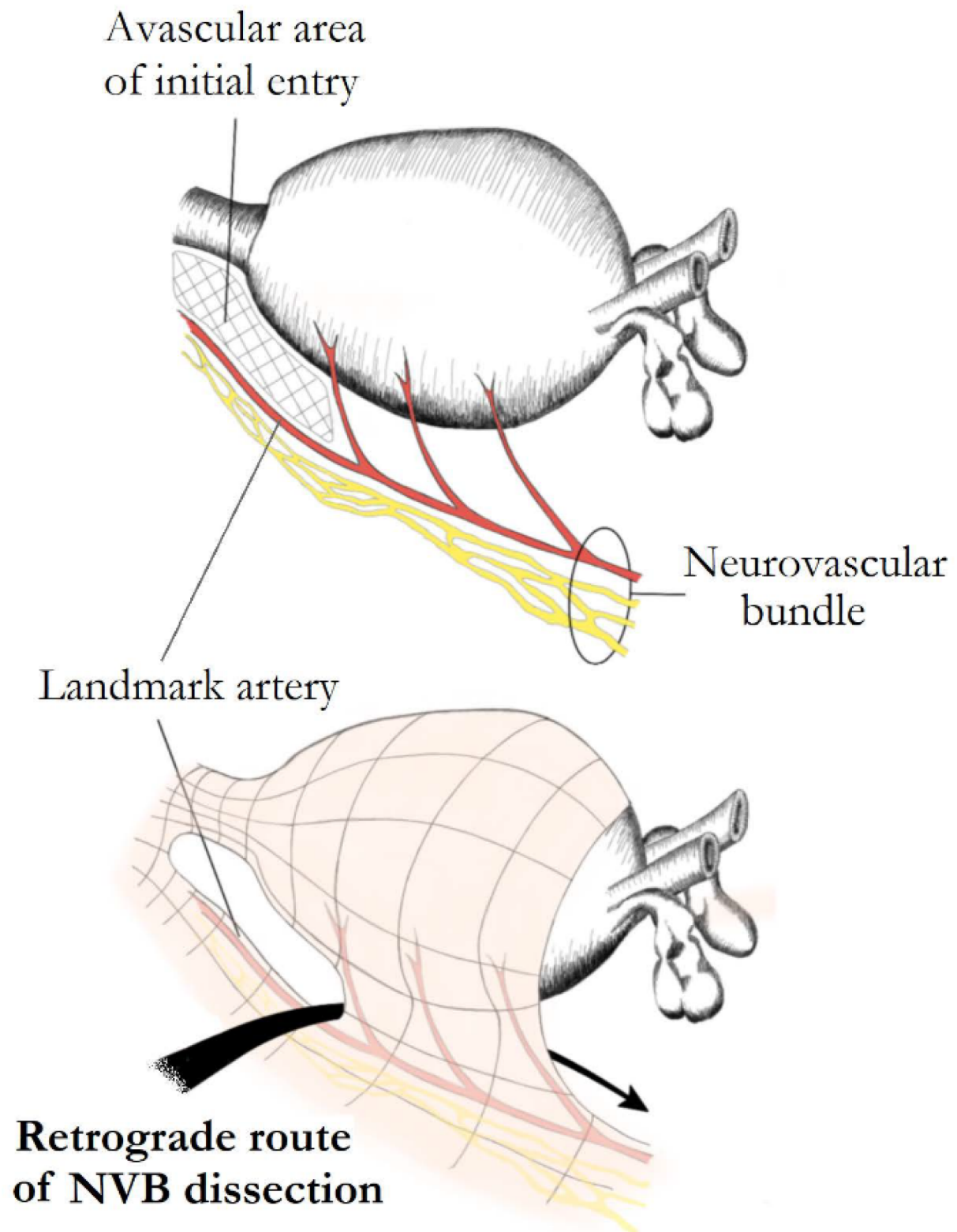


Figure 3. Retrograde nerve-sparing. After posterior prostatic dissection, an avascular area at the lateral margins of the prostatic apex overlying the landmark artery (LA) of neurovascular bundles is identified and used as the initial point of dissection. The bundles are further dissected in a retrograde fashion. Preservation of the LA ensures complete preservation of the ipsilateral main neural branch.

Conversely, in the antegrade approach, the direction of the dissection is from the prostatic base towards the apex with the vascular pedicles being transected first [1][14]. Antegrade NS is a widely used practice among laparoscopic and robotic surgeons. The procedure starts with gentle upward traction of the vas and seminal vesicles in order to reveal the prostatic pedicles. Counter traction of the prostate exposes the triangular space between the lateral pelvic fascia, the Denonvilliers' fascia and the prostatic fascia and either the interfascial or the intrafascial dissection is performed [13][14]. An antegrade approach has been described in open surgery as well [15][16]. According to Carini et al., open antegrade NS constitutes a less challenging procedure with similar results to those reported by the retrograde approach [15]. Finally, a partial retrograde approach has been described which preserves the advantages of the antegrade NS, but takes the vascular pedicles last as in the retrograde NS [1].

Regarding the impact of different directions of NS on functional outcomes, a questionnaire-based assessment demonstrated that 67% of patients undergoing retrograde, and 76% of patients undergoing antegrade NS laparoscopic RP, were able to engage in sexual intercourse (with or without phosphodiesterase-5 inhibitors) postoperatively [17]. On the contrary, in a nonrandomized comparative study, Ko et al. reported that, in patients with normal preoperative erectile function, a retrograde direction of nerve-sparing during RARP was associated with significantly higher potency rates at 3, 6 and 9 months compared with an antegrade direction of NS, without compromising cancer control [18].

4. The Functional Impact of Using Energy and Nerve Traction during NS RP

The potential injury and functional recovery of the nerves depend first of all on the nature of the nerves. While some studies have failed to identify myelinated nerve fibers originating from inferior hypogastric plexus [19], others have shown both myelinated and unmyelinated components in prostatic nerves [20][21]. There are several classifications used for evaluating and terming nerve injuries [22]. Based on Seddon's classification, the nerve injuries can be divided into 3 types: neurapraxia, axonotmesis and neurotmesis [23]. Neurapraxia is a first-degree injury, commonly caused by mechanic blunt trauma to the nerves. The recovery after this injury may take as long as 12 weeks. Axonotmesis, the second-degree injury, is termed so due to axonal injury, yet preserving the surrounding connective tissue. Depending on the injury distance and with the axonal growth rate of 1 mm/day delayed nerve recovery, up to 24 months may be required. Neurotmesis is the most severe injury of the nerve commonly resulting in an irreversible loss of nerve function [24].

The nerves of NVBs, are sensitive to thermal energy which is diffused during current use in adjacent structures [2]. Suspecting that thermal injury of NVBs could be responsible for the postoperative loss of potency, many investigators tried to develop totally athermal methods. Theoretically, cautery-free techniques manage adequate hemostasis, while improving the return of erectile function by minimizing injury to the NVBs. Vascular clips, suture ligation and bulldog clamps with suturing constitute the most common cautery-free techniques, used during prostatic vascular pedicle manipulations [1]. In addition, several hemostatic agents have been used for the purpose of controlling bleeding. Although hemostatic agents were used in Ahlering's initial report, their inability to manage hemostasis in 15% of the cases led to their substitution by suture ligation [25]. Gill et al. also reported problems with

FloSeal™ in their laparoscopic RP series, frequently requiring secondary clip placement [26]. Moreover, usage of bioadhesives near the NVBs can potentially injure them, as a result of a lymphocytic inflammatory reaction and fibrosis [1].

The impact of different hemostatic energy sources on the integrity of NVBs was initially documented in the experimental setting. Ong et al. evaluated cavernous nerve function on 12 dogs, which were divided into 4 groups, each subjected to NS using conventional dissection with suture ligatures, monopolar electrosurgery, bipolar electrosurgery or ultrasonic shears, respectively. The authors observed that the use of energy sources near the NVBs was associated with a considerable decrease in erectile response both acutely and after 2 weeks; while following conventional dissection with suture ligatures, the erectile response to nerve stimulation was unaffected [27]. It has been also shown that monopolar and bipolar energy have an almost similar risk of heat generation and potential tissue injury [28]. However, a decreased risk of nerve injury with bipolar energy can be observed when cut and cauterization is performed, so-called touch cautery, due to preservation of adjacent blood flow [29].

In accordance with these findings, several clinical studies confirmed the importance of athermal dissection. Ahlering et al. described a clipless cautery-free approach for NS, using bulldog vascular clamps and sutures, and reported a nearly 5-fold rate of improvement in potency recovery as compared to a group where NS took place using cautery. Defining potency as “erectile hard enough for vaginal penetration with or without the use of PDE-5 inhibitors” in the cautery group, 14.7% of patients were potent after 9 months and 63.2% after 24 months, as compared to 69.8% (after 9 months) and 92% (after 24 months) for the cautery-free group [25][30][31]. Likewise, Chien et al. described analogous findings during a completely athermal RARP procedure, reporting a faster return and preservation of sexual function. In their modified clipless antegrade NS technique, after developing the posterior plane of the prostate towards the apex in the midline, they released the vascular pedicles and the NVBs in a medial-to-lateral direction using a combination of sharp and cold scissors. They only used judiciously bipolar cautery, avoiding clips and monopolar cautery. According to them, the potency rates after this approach, using a 36-item health survey questionnaire, were 47%, 54%, 66% and 69% after 1, 3, 6 and 12 months, respectively [32]. Gill et al. using real-time Doppler transrectal ultrasound showed that bulldog clamping of the lateral vascular pedicles was associated with preservation of blood flow in the NVBs and restriction of the need for cautery [26]. Finally, Fagin et al. compared three different NS techniques (selective bipolar cautery, an athermal “clip and peel” posterior dissection technique and an athermal combined anterior and posterior dissection technique with clips and sharp dissection). The authors reported better recovery of potency with the athermal techniques, with the combined anterior and posterior approach being the superior of the two athermal techniques. This approach was also associated with the lowest positive margin rates [33].

Regarding the impact of different energy sources on functional outcomes, the available data are limited. Pagliarulo et al. compared the athermal and the ultrasonic NS laparoscopic RP procedures, coming to the conclusion that the use of an ultrasonic device did not have a negative impact on long-term potency and continence outcomes, nor did it lead to early biochemical recurrence, as compared to the athermal approach [34]. Pastore et al. performed a prospective randomized study, comparing radiofrequency and ultrasound scalpels on functional outcomes of

laparoscopic RP and documented that the radiofrequency scalpel was associated with better functional outcomes [35].

With regard to the impact of traction on the integrity of NVBs, many studies have documented the positive effects of traction-free techniques. Kowalczyk et al. observing 610 patients who underwent RARP, 342 of whom were with avoidance of countertraction of the NVBs during NS, reported earlier sexual function recovery in the traction-free group (45% versus 28% at five months). However, potency rates were the same among the two groups at 1 year [36]. Similar results were reported by Masterson et al., who modified their technique in order to avoid countertraction of the NVBs during RARP and observed improved rates of erectile function recovery during a six-month period [37]. Finally, Mattei et al. presented the results of their lateral approach for the interfascial dissection of the NVBs without tension and any use of electrocautery. In their study, one week after catheter removal, 80% of patients had complete early urinary continence and a high rate of patients reported spontaneous erections or penile tumescence, while at the 4-month follow-up visit, 92.4% of patients were completely continent and 65% of patients were considered potent [38].

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