Pelvic Neuroanatomy and Radical Prostatectomy with Neurovascular Preservation: Quo Vadis?

Several studies in the literature have established that appropriate surgical excision of the prostate gland and seminal vesicles halts cancer progression and provides long-term survival for men with clinically localized prostate cancer. But the impact of the surgical technique on a potent patient, with any of the different approaches (open, laparoscopic, robotic, or perineal), involves rates of erectile dysfunction that are far from acceptable.

In the early 1980s, Walsh and Donker [1] and Walsh et al [2] described the anatomic location of the cavernous nerves—the neurovascular bundle (NVB)—and delineated a surgical technique to preserve them. This technique opened the way toward the ultimate goal of removing the tumor while maintaining the integrity of these nerves, thus allowing the patient to reestablish his sex life.

Undoubtedly, the accurate location of the NVB is critical to preserving it. The location of the NVB that was presented in 1982 went unchallenged through the 1980s and 1990s. The location of the NVB was limited to the posterolateral prostate area, between the two sheets of the pelvic lateral fascia known as *levator* and *prostatic* fascia [2], and improvements in surgical technique that enhanced NVB preservation were reported.

Early in this century, the cadaveric studies by Takenaka et al [3,4] and Costello et al [5] challenged the paradigm by suggesting that branches of the pelvic plexus (parasympathetic erection) could be traced in an anterior lateral location, much anterior to the original location described by Walsh and Donker [1]. The scientific community was in upheaval in 2006 as these anterolateral branches that went very close to the apex were described as the "veil" by Menon et al [6]. These investigators described their preservation technique, reporting incredible outcomes: 1-yr potency rate of 96%, with 71% of patients returning to what they considered their previous sexual quality of life. This technique includes an intrafascial dissection in both the posterolateral and the anterior area of the prostate, that is, between the prostatic fascia and pseudocapsule (intrafascial) [6,7]. Additionally, the extension goes from the bladder neck to the prostatic apex in the lateral zone. Importantly, these results did not come from randomized trials and have not been validated. Nevertheless, intriguing questions were raised about whether this *anterior leaf* of the NVB may portend such a strong effect on erectile function outcomes.

Two recent investigations suggested modifications that preserve these anterorateral branches of the NVB by either retrograde (apex to base) [1] or antegrade [8] release. Both of these reports had consistent 1-yr potency rates of 70% [1,2].

The antegrade dissection described by Nielsen et al as "high anterior release of the levator fascia" [8] consists of releasing the whole anterolateral and posterolateral periprostatic tissue by medially opening the levator fascia close to the insertion of the puboprostatic ligaments in the prostate anterior face. This approach separates the anterolateral tissue and the NVB from the prostatic surface represented by the prostatic fascia. The retrograde approach accomplishes the same goal. For both approaches, the dissection level is between the levator fascia and the prostatic fascia (ie, interfascial).

On reflection, three major points are worth discussing. First, it is critical to dissect the plane between the prostate and the periprostatic fascia, specifically between the apex and the middle-lateral zone. Takenaka et al [9] showed that fibers of the parasympathetic pelvic plexus enter the NVB approximately 2 cm distal to the vesical prostatic junction (neck) [10]. This finding suggests that the medial and distal dissection is crucial for nerve sparing but that the proximal dissection is not. Thus, a difference is clear between the *high release* [8] and veil [11] techniques: The high release begins just proximal to the middle of the prostate gland and extends to the urethra, while the veil technique begins at the bladder neck. Despite the lack of randomization, the literature suggests that both techniques achieve similar results. This similarity raises questions about the importance of this technical detail.

Second, the work by Costello and colleagues [5] defines those nerves in close intimate relationship with the prostatic pseudocapsule and fascia as prostate nerves, not cavernous nerve branches. The study by Nielsen et al [8] addressed this point, and the authors suggested that dissection should be undertaken on the lateral-outside of the prostatic fascia. The research from Takenaka et al [12] further supports this plane of dissection. When these investigators stimulated the established NVB (posterolateral area), the intracavernous pressure increased in contrast to increases of the intraurethral pressure but not the intracavernous pressure when the anterolateral area was stimulated. They concluded that these anterior fibers do not seem to be cavernous nerve branches. These investigations contrast sharply with the theory of intrafascial preservation of the lateroprostatic fascia "Veil" study [7], which emphasizes the importance of preserving the nerve endings that are beneath the prostatic fascia (ie, between the fascia and the prostatic pseudocapsule). Additionally, Kaiho and colleagues [13] showed recently in a very elegant study that stimulating anterior and lateral circumference of the prostatic capsule increases cavernosal pressure. The dispute is served by a randomized clinical trial powered for measuring erectile function recovery and the competing event of a positive surgical margin.

Third, a plausible explanation for the incremental erectile recovery after surgery may not be dependent on the anterolateral fibers but rather on a decreased trauma in the posterolateral NVB provided by change in the dissection of periprostatic tissues. Antegrade or retrograde early release of the apex and midgland periprostatic tissues immediately after opening endopelvic fascia may prevent dissection *traction* on the NVB. This lack of traction on the NVB may prevent trauma due to elongation. Montorsi et al [14] tested and supported this hypothesis in their respec-

tive series [15,16]. Perhaps this technical amendment could explain the identical results independently reported by authors performing the procedure unilateral or bilaterally.

Understanding of the nervous structures that anatomically surround the prostate continues to expand. Clinical trials are needed to generate evidence-based conclusions that lead to more accurate surgical execution and patient counseling.

Conflicts of interest: The authors have nothing to disclose.

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Estrogen and Progesterone Hormonal Receptor Expression in Urothelial Carcinoma of the Bladder

Urothelial carcinoma of the bladder (UCB) is nearly three times more common in men than in women, but women present with more advanced stage and have lower survival rates [1]. Although these differences have been primarily attributed to differences in exposure to smoking and industrial chemicals, it is evident now that genetic, anatomic, societal, and hormonal factors also play a role. One of the explanations for the differential biologic behavior of UCB between men and women has focused on sex steroid hormones and their receptors. If hormone receptors are differentially expressed between genders and/or contribute to the biologic aggressiveness of UCB, they could serve as targets for prevention or treatment of UCB.

The expression of estrogen receptor (ER) and progesterone receptor (PR) plays an important role during development, growth, tumorigenesis, and progression of several malignancies, offering a rationale for targeted therapy [2]. In breast cancer, ER and PR status are established prognostic factors helping in the identification of patients likely to benefit from antihormonal therapy. UCB cell lines express