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INVITED REVIEW

Neural supply of the male urethral sphincter: comprehensive anatomical review and implications for continence recovery after radical prostatectomy

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Abstract
Purpose To review the anatomical facts of urethral sphincter (US) innervation discovered over the last three decades and to determine the implications for continence recovery after radical prostatectomy (RP).
Methods Using the PubMed® database, we searched for peer-reviewed articles in English between January 1985 and September 2015, with the following terms: 'urethral sphincter,' 'urethral rhabdosphincter,' 'urinary continence and nerve supply' and 'neuroanatomy and nerve sparing.' The anatomical methodology, number of bodies examined, data, figures, relevant facts and text were analyzed.
Results Seventeen articles on 254 anatomical subjects were reviewed. Coexisting pathways were described in every article. Dissection, histology, simulation or electron microscopy evidence supported arguments for somatic and autonomic pathways. From the most to the least substantiated, somatic sphincteric fibers were described extra- or intrapelvic as: direct from the distal pudendal nerve (PuN), recurrent from the dorsal nerve of the penis, from the proximal PuN with an intrapelvic course, extrapudendal somatic fibers dispersed among autonomic pelvic fibers. From the pelvic plexus, or from the neurovascular bundles, autonomic fibers to the US have been described in 13 of the reviewed articles, with at least each of the available anatomical methods.
Conclusion Because continence depends on a number of factors, it is challenging to delineate the specific impact of periprostatic nerve sparing on continence, but the anatomical data suggest that RP surgeons should steer toward the preservation and protection of these nerves whenever possible.

Keywords Nerve sparing · Innervation · Prostate · Urinary continence

Abbreviations

DNP	Dorsal nerve of the penis
IHP	Inferior hypogastric plexus
LAM	Levator ani muscle
LAF	Levator ani fascia
LAN	Levator ani nerve
PPx	Pelvic plexus
PSN	Pelvic splanchnic nerve
PuN	Pudendal nerve
RP	Radical prostatectomy

Introduction

Continence is a variable of the 'trifecta' outcome following radical prostatectomy (RP), and its recovery is a crucial issue postoperatively. The urethral sphincter (US) plays a critical role in urinary continence after radical prostate

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cancer surgery [1]. Like any other musculature, its optimal function requires maintenance of supporting structures and functional muscular mass, as well as proper angulation and neural coordination for periodic relaxation and prolonged constriction. While the US anatomy has been studied extensively, its nerve supply and coordinated function is far from clear, as there are long-lasting conflicting hypotheses about the nature and course of its nerves [2–4].

Some researchers reconcile different views by suggesting that the US may be supplied by a combination of somatic and autonomic innervation or that possible neural communications may optimize and coordinate functioning [5]. Some have gone on to propose triple innervation involving somatic, parasympathetic and sympathetic supply [6]. It has even been suggested that somatic innervation would travel through the pelvic plexus, thereby facilitating a non-pudendal nerve course for somatic fibers [7]. In addition to the source of innervation, lack of detailed knowledge of the course of the relevant nerves remains a stumbling block for prostate cancer surgeons trying to improve functional outcomes after RP.

Regardless of the surgical approach—open [8, 9]/laparoscopic [10, 11]/robotic [12, 13]—or of the year of publication, the controversy about the effect of nerve sparing on continence continues and remains a topic of much debate. Reeves et al. have recently reviewed 13,749 RP in 27 studies and reported that nerve sparing was improving continence only in the first 6 months [14]. However, a recent prospective and multicenter study has reported an association between the degree of bundle preservation and urinary incontinence 1 yr after open or robotic surgery [15].

It is likely that return of continence is a multifactorial process involving coordinated muscular contraction of the sphincteric complex, a compliant and capacious detrusor reservoir, optimal angulation and support of the vesico-urethral junction, vascularity and suppleness of the vesico-urethral anastomosis, length of the sphincteric tube, type and duration of the drainage, and the patient's age. Herein, we review the important clinical anatomy of the neural supply to the urethral sphincter and discuss the implications for continence recovery during radical prostatectomy.

Methods

To comprehensively review the neuroanatomy of the urethral sphincter, we searched the PubMed database for articles published in English from January 1985 to September 2015 using each of the following keyword: 'urethral sphincter,' 'urethral rhabdosphincter,' 'urinary continence' in combination (Boolean operator [AND]) with each of the following terms: 'innervation,' 'nerve supply,' 'neuroanatomy,' 'nerve sparing.' No other PubMed filter than English language was used. The selection was then made by the first and last authors. First, a negative selection was made by reading the abstracts: animal studies, non-anatomical methodology, surgical series and case reports were excluded from the review. Second, a positive selection was made by reading the articles: dissections of several adult bodies, histological analyses or reconstructions of several adult bodies or fetuses, intraoperative stimulations studies were included in the review. Third, another similar selection process was made on: the first 5 'similar articles' suggested by PubMed for each of the formerly selected articles, and on each of its references published between January 1985 and September 2015. To ensure a comprehensive review, the following data were noted for each of the selected articles: anatomical methodology, number and gender of bodies examined, data, type of figures, relevant facts and text. Relevance was appraised in consensus between first and last authors and defined as: anatomical facts in relation with the innervation of the US. The information was grouped into somatic and autonomic innervations. For each pathway, a semiquantitative (from 0 to +++++) evaluation of quality of the reviewed data was performed for: number of subjects (none; 0–10; 10–30; 30–90; 90–200; > 200), illustrations (none; low-resolution image in 1 study; low-resolution images in several studies; high-resolution image in 1 study; high-resolution images in several studies); histology (none; tissue staining; solely an aspecific neural antibody (PS100); 1 autonomic antibody; several autonomic antibodies); electronic microscopy (none; axonal morphology criteria in 1 study; axonal morphology criteria in several studies; neuron or tissue analysis associated in 1 study; neuron or tissue analysis associated in several studies). Presented herein are the findings of this comprehensive review.

Results

Seventeen articles have been selected for review. Articles solely based on per-operative data, articles based on less than three anatomical subjects and data acquired on women or female fetuses were excluded from the review. Results were organized into a comprehensive anatomical presentation based on the main possible neural pathways that

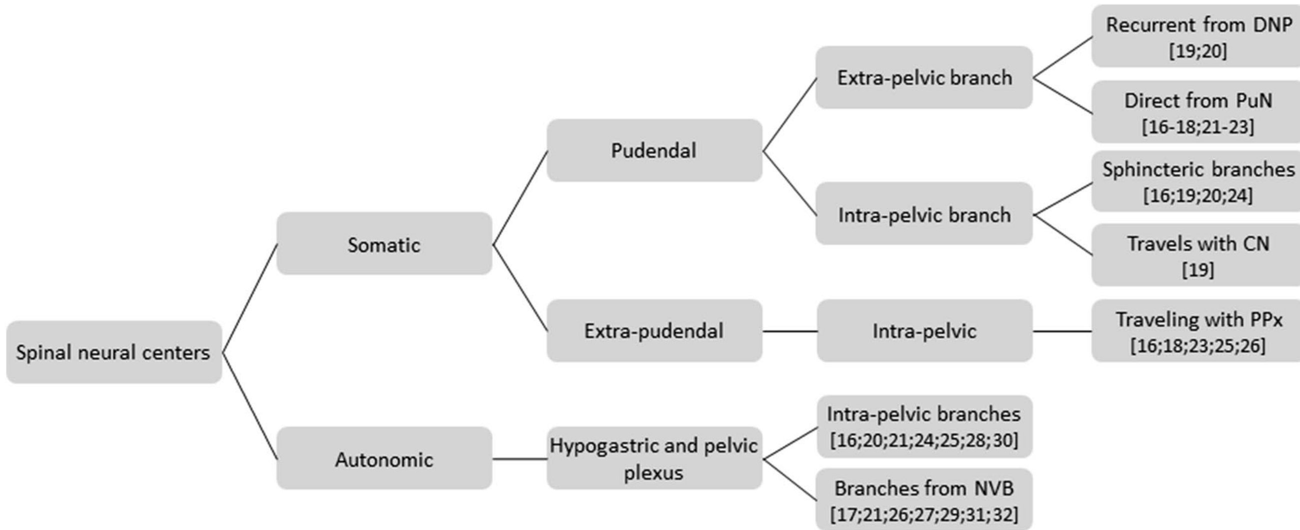

Fig. 1 Potential neural pathways to urethral sphincter (US) innervation

supply the US: somatic, autonomic and communicating branches (Fig. 1). For each, we will discuss the possible course of nerves according to the current literature.

Somatic innervation

The somatic motor innervation of the US arises from the cell bodies of sacral spinal cord segments S2–S4 and is organized in Onuf's nucleus. The somatic branches travel to the target structures either through branches of the pudendal nerve or through nerves that travel with branches of the pelvic plexus. The nerves to the male US can be classified as either extrapelvic branches of the pudendal nerve, intrapelvic branches of the pudendal nerve or branches of the inferior hypogastric plexus (IHP).

Pudendal pathways: extrapelvic branches

Eight anatomical studies based on 108 conventional dissections of adult male bodies and the histological examinations of 7 fetuses have described the extrapelvic pudendal pathway (Table 1; Fig. 2) [16–23]. This is the most established neural pathway for the extrinsic US (EUS). The PuN, after its origin, travels through the greater sciatic notch to course anteriorly within the pudendal canal (of alcock). The ischial spine is a common anatomical landmark in all anatomical studies. PuN branches provide the inferior rectal, perineal, posterior scrotal and sphincteric nerve fibers. A first set of sphincteric fibers commonly enters the prostatic urethra at the 9–12 o'clock and 1–3 o'clock positions, less than 10 mm away from the prostatic apex, making them at risk for damage during apical dissection. A second set of sphincteric fibers branches from the dorsal nerve of the penis and reaches the sphincter retrogradely, in an anterolateral position, making them at risk for damage during the dorsal vein complex stitching.

Pudendal pathways: intrapelvic branches

Four anatomical studies based on 81 conventional dissections of adult male bodies have described the intrapelvic pudendal pathway (Table 2; Fig. 3) [16, 19, 20, 24]. The intrapelvic branches exit, while the PuN is in the pudendal canal, and they travel through the levator ani muscle (LAM) toward the EUS near the prostatic apex. Intrapelvic branches of the PuN enter the EUS at a 5 or 7 o'clock positions. In the largest studies, this pathway is highly variable and only observed in 30–40 % of the dissections whereas the most constant (60 % under the operating microscope) pathway remains extrapelvic.

Table 1 Somatic pudendal extrapelvic nerve pathways to the US

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
1995	Narayan, *J Urol* [19]	Gross dissection + histology	18	Adult bodies	Recurrent branch from DNP, 0.3 to 1.3 from prostatic apex, positioned anterolateral to the US and entering 9–12 o'clock and 1–3 o'clock positions	Photographs	Risk at apex dissection or during stitching the dorsal vein complex
1988	Jueneman, *J Urol* [18]	Gross dissection + 5 stimulations in neurogenic LUT dysfunction patients	3	Adult bodies	Branches of the PuN to the EUS originates dorsolaterally, opposite the anal sphincteric branches and shortly after the pudendal nerve crosses the sacrospinal ligament and ischial spine; electrostimulation of the pudendal nerve markedly increased intraurethral closure pressures	Photographs + urethral pressure	Authors do not *believe* that the neural control of the EUS is autonomic
1994	Zvara, *Br J Urol* [23]	Gross dissection	6	Adult bodies	1–4 Direct branches from the PuN to the striated US, originated 1–1.5 cm after the ischial spine, approached the US from the dorsolateral aspect, and dived into the dorsal part of the US 0.8–1.1 cm from the lateral wall of the urethra	Photographs	Risk of injury during apical dissection
2000	Strasser, *World J Urol* [21]	Gross dissection + 22 male patients transurethral ultrasound of the US complex	14	Adult bodies	Branches of the PuN given off lateral to the EUS and reach the muscle at its dorsolateral aspects; the mean distance from the membranous urethra to the point of entry of these fine fibers into the EUS is 0.5–1.1 cm	Photographs	Predominantly innervate the lower part of the urethra, namely the rhabdosphincter
2003	Akita, *Surg Radiol Anat* [16]	Gross dissection	44	Adult bodies	Small twigs from the PuN extended to supply the US muscle region from the anterolateral surface (inconstant, 60 %)	Photographs	It is sometimes impossible to observe (even under the operating microscope) the branches to the US muscle region from the PuN: Therefore, in some specimens the region is mainly innervated by the branches of the PPx
2005	Takenaka, *BJU Int* [22]	Gross dissection	8	Adult bodies	Small branches from the PuN reached the EUS, 5.5 mm from the lowest point of the LAF	Photographs	After exposing the LAM fibers beneath its fascia, the nerve was vulnerable to injury
2010	Song, *Neurourol Urodyn* [20]	Gross dissection	15	Adult bodies	The extrapelvic branches originated from the DPN to innervate the membranous urethra, 4.2 mm from the prostatic apex (inconstant, 53 %)	Photographs	Injury to these nerves may occur during apical dissection of the prostate

Table 1 continued

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
2011	Alsaid, *J Anat* [17]	Histology	7	Fetuses	The EUS received different branches of the PuN arising just before its penetration of the urogenital diaphragm	PMP22 labeling + CAAD	Retroapical surgical risk

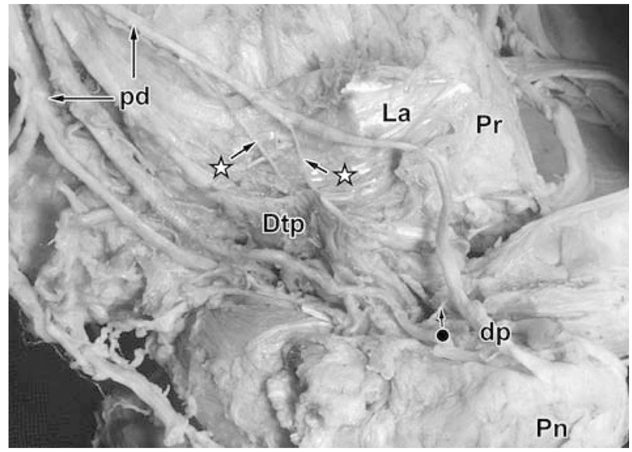

Fig. 2 Pudendal pathways—extrapelvic branches. Branches of the pudendal nerve in the perineum after removal of the coxal bone. Lateral aspect. The branch to the urethral sphincter region from the dorsal nerve of the penis is shown (*black dot*), and the branches to the deep transverse perinei are observed (*white star*). *Bl* bladder, *dp* dorsal nerve of the penis, *Dtp* deep transverse perinei muscle, *La* levator ani muscle, *pd* pudendal nerve, *Pn* penis, *Pr* prostate. Exact caption from the original article by Akita et al. used with permission [16]

Non-pudendal pathways

Five anatomical studies based on 88 subjects were reviewed. Three studies with 53 conventional dissections in adult bodies have illustrated that some of the somatic sacral 2, 3 and 4 branches arise from the lowermost root of the pelvic splanchnic nerve and travel with the autonomic fibers of the pelvic plexus and innervate the US (Table 3; Fig. 4) [16, 18, 20, 23, 24]. In two studies based on the examination of 35 fetuses, Karam et al. [25] and Takenaka et al. [26] observed and distinguished both myelinated and unmyelinated nerve fibers traveling along the bladder neck to the urethra, suggesting dual innervation of these structures. All fibers were at the posterior face of the bladder neck and followed the same course, penetrating the US: from its anterolateral surface for the myelinated fibers classically considered as somatic; from its posterolateral surface for the unmyelinated fibers classically considered as autonomic. The non-pudendal somatic pathway to the US has been conceptualized by Akita [16].

Autonomic innervation

Thirteen studies involving 219 subjects (adult bodies, deceased fetuses or living patients) have, over the years, progressively raised the level of evidence to support the role of autonomic nerve fibers in EUS innervation (Table 4; Fig. 5) [16, 17, 20, 21, 24–32]. Conventional dissections have been the first method to identify nerve fibers reaching the EUS from the neurovascular bundles (NVBs).

Table 2 Somatic pudendal intrapelvic nerve pathways to the US

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
1995	Narayan, *J Urol* [19]	Gross dissection + histology	18	Adult bodies	Perineal branches of the posterior portion of the PuN, close to the anal branches; luxol fast blue stain typically revealed a bubble-like pattern characteristic of somatic myelinated fibers	Photographs + LFB staining	May be stretched by an excessive traction of the prostate
1997	Hollabaugh, *Urology* [24]	Gross dissection	4	Adult bodies	Intrapelvic branch of the PuN is a putative continence nerve that enters the EUS at the 5 and 7 o'clock positions, deep to the LAF	Photographs	Injury to the innervation of the EUS is avoided by not spreading with a right-angle clamp between the EUS and rectum and by transecting the rectourethralis muscle at the prostatic apex after the NVB have been released from the prostatic apex
2003	Akita, *Surg Radiol Anat* [16]	Gross dissection	44	Adult bodies	A small twig from the PuN, which pierced the LAM and fused with the branch to the rhabdosphincter, was observed (inconstant, 20 %); a branch of the LAN pierced the LAM and fused with the PuN (inconstant, 30 %)	Photographs	This pathway is piercing the LAM
2010	Song, *Neurourol Urodyn* [20]	Gross dissection	15	Adult bodies	Before exiting the pudendal canal, the PuN gives off an intrapelvic branch that traverses the LAM to course with the pelvic nerve to innervate the membranous urethra (inconstant, 40 %) at an the average distance of 5.3 mm from the prostatic apex	Photographs	The branches of the DNP are suggested to be responsible for urinary continence; impaired seemed to be associated with membranous urethral sensitivity, particularly in patients with occasional urinary leakage

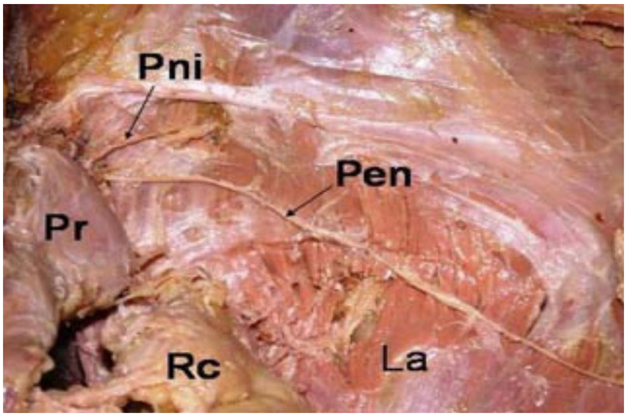

Fig. 3 Pudendal pathways—intrapelvic branches. Pelvic nerve and intrapelvic branches of pudendal nerve (*right*). *Rc* rectum, *Pr* prostate, *Pni* intrapelvic branches of pudendal nerve, *Pen* pelvic nerve, *La* levator ani. Exact caption from the original article by Song et al. [20] used with permission

These fibers were observed at the posterolateral aspects of the prostate apex, along the rectum covered by the LAF, as they originate from the most caudal edge of the inferior hypogastric plexus (IHP) or from the neurovascular bundle (NVB) itself. Basic histological studies have then established the unmyelinated feature of these fibers, which was an argument in support of their autonomic nature. With more refined immunolabelings and electron microscopy, it has been possible to characterize sympathetic and parasympathetic fibers to the EUS. Few intraoperative electrophysiological studies have also given credit to the hypothesis that the NVB contains sphincteric fibers, as the intraurethral pressure increases in response to electrical stimulation.

Somatic–autonomic communications

Five of the previously reviewed studies have illustrated and classified topographical communications between the somatic (infralevator) and the autonomic (supralevator) pathways in 95 adult bodies or fetuses (Table 5; Fig. 6) [16, 17, 20, 24, 26]. The more proximal one follows these fibers, the more communications were constant (94 %); the more distal, the less communications were constant (10 %). A common trunk to the LAN and the PSN was the first and the most consistent shared pathway by different nerve fibers. The levator ani muscle (LAM) also appeared to be a crucial anatomical structure as it is pierced by fibers from the autonomic and somatic systems, and it could thus have an underestimated role in urinary continence. The urethral sphincter was described as uniquely innervated through both autonomic and somatic innervations that may coordinate the complex function of urinary control and voiding during a wide variety of stress and bladder filling [17].

Discussion

The US is assimilated to a muscular complex with smooth and skeletal muscle fibers involved in passive and active continence [33]. Specifically, the external US is said to be more amenable to prolonged contractions. It envelops the prostate and urethra from the vesical orifice base to the membranous urethra. This crescent-shaped structure above the verumontanum transitions into a horseshoe shape wherein the muscle is thickest ventrally [34]. The rectourethralis muscle and external US are in juxtaposition, and along with the levator ani muscle and the bulbospongiosus muscle, converge along the median fibrous raphe. Though they are very close in proximity, a distinct layer of connective tissue separates the levator ani muscles and external urinary sphincter muscle [35]. US innervation has long been reduced to a somatic pudendal extrapelvic nerve supply, and the present review rather pleads for a complex or a variable innervation. With as many descriptions as reviewed articles, consensus regarding the urethral sphincter's innervation has not been reached over the last three decades. We have comprehensively reviewed the anatomy and evidence from all relevant studies in this article. The elegant reconstruction by Stolzenburg's team (Fig. 7) and the informative schema by Akita et al. (Fig. 8) have enabled an anatomical-surgical conception of the US innervation pathways (Fig. 9) [16, 36, 37].

By comparing all of the selected studies, we were able to estimate different degrees of certainty regarding each anatomical claim. Credibility was estimated by the number of subjects and studies, the extent of the dissections, the quality of the illustrations, the study design, the methodologies and the antibodies' reliability at the time of publication, the logical reasoning and even the vocabulary used by authors in their demonstration, which we summarized in a gray-scale reading template (Table 6). In particular, great

Table 3 Somatic extrapudendal nerve pathways to the US

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
1988	Jueneman, *J Urol* [18]	Gross dissection + stimulation in 5 patients with neurogenic LUT dysfunction	3	Adult bodies	A few somatic branches to the EUS primarily emanate from S2 and S3 ventral roots, run close to the PPx to innervate the EUS; electrostimulation of the sacral root markedly increased intraurethral closure pressures (almost 70 % of the closure pressure of the EUS is induced by stimulation of the S3 ventral root)	Photographs + urethral pressure	S2 and S3 somatic nerve fibers interrelate and crossover in the EUS innervation
1994	Zvara, *Br J Urol* [23]	Gross dissection	6	Adult bodies	2–5 Branches following PPx and diving to the striated US, 3.2 cm from urethral wall (inconstant, 83 %)	Photographs	May explain residual sphincteric contraction that remains after peripheral neurotomy of the PuN
2003	Akita, *Surg Radiol Anat* [16]	Gross dissection	44	Adult bodies	From PPx, running on LAM (constant, 100 %)	Photographs	It can only be suggested that somatic nerve fibers might also run along the branches from the PPx
2005	Karam, *Eur Urol* [25]	Histology	10	Fetuses	Myelinated fibers at the inferolateral aspect of the prostate enter the US from the anterolateral surface at 3 and 9 o'clock	LFB staining + CAAD	The identification of myelinated fibers following unmyelinated fibers from bladder neck to the EUS suggests that few somatic nervous fibers could have an intrapelvic course
2005	Takenaka, *Urology* [26]	Gross dissection + histology	25	Adult bodies	Twigs from the CN to the sphincter area contained myelinated fibers nearly 10 μm in diameter, as demonstrated by Luxol fast blue staining	LFB staining + histology	Myelinated fibers were likely to correspond to the motor innervation of the rhabdosphincter: preservation of the CN should also accomplish the preservation of the intrapelvic continence fibers

Fig. 4 Non-pudendal pathways. Branches from the sacral roots to the levator ani running inside the pelvis—cadaveric dissection. Exact caption from the original article by Zvara et al. [23] used with permission

attention was paid to the histological protocols. Conclusions drawn on multicontrolled immunolabels [17] were considered more reliable than simple stainings [19, 25, 26], whole-pelvic studies were rated higher than restricted regions of interest on the EUS [25, 30], and intraoperative stimulations [18, 31] were more valuable than postoperative stimulations [27].

In the controversy of EUS innervation, anatomical facts add up and strengthen the possibility of a somatic and autonomic co-innervation. In the 1980s, little credit was given to an autonomic component of the EUS innervation because anatomical evidence was missing, but it was not factually excluded. In the 2010s, the debate is still ongoing but, with cumulative evidence for nerve supply to the EUS through both autonomic and somatic innervation, it seems the burden of proof has changed. In the meantime, the anatomical concept of a sole innervation for a striated muscle is also changing for the LAM [29]. An autonomic participation to the LAM innervation is now described and a coordinated role of the LAM and the EUS, both eventually being mixed autonomic and somatic-innervated, becomes consistent. Autonomic innervation originates from the hypogastric and pelvic plexuses, whereas somatic innervation arises through both pudendal and non-pudendal branches. These branches may play a role in preventing muscle fatigue and thereby facilitate the early return of urinary continence [29]. These branches supply not only the sphincter but also supporting muscles such as the levator ani and rectourethralis, which can contribute to continence indirectly.

In the reviewed descriptions, different anatomical landmarks appeared of noteworthy surgical interest. Serving as a boundary between intra- and extrapelvic branches, the fascia of levator ani (FLA) has its lowest point at a mean distance of 5 mm from the sphincteric branch. The distance between the pelvic floor and the nerve entry point decreases with opening and exposure of the LAM fibers beneath the FLA, thus making sphincteric nerve fibers vulnerable to injury during pelvic floor surgery [22]. At the prostate apex, the extrapelvic somatic sphincteric branches enter the EUS at a distance of ranging from 4 to 11 mm, with risk for damage during apical dissection [20, 21, 23]. Steiner has refined surgical techniques to minimize stress manipulation of the EUS and to preserve these nerves in the name of continence preservation [38]. At the era of open prostatectomy, he recommended to avoid using a right-angle clamp to establish the plane between the posterior urethra and underlying rectourethralis and median fibrous raphe, and his concept remains timely for laparoscopic and robot-assisted RP.

The return of continence following RP is a multifactorial process [39] that involves the length (and bulk) of the urethral sphincter, integrity of supporting structures, appropriate angulation, proper functioning of the bladder as a reservoir, correct technique of the vesico-urethral anastomosis, disruption of the retropubic space and reperitonization of the bladder in its normal location. Over time, the body attempts to heal these anatomical changes, and continence recovers in the majority of cases. Technical refinements that target early return of continence vary. Techniques include preservation of the bladder neck, reconstruction of the posterior support, reconfiguration of the bladder opening, and realignment and reconstruction of supporting ligaments. Several authors have advocated anterior, posterior and total reconstruction to assist in early return of continence. It may be that like other factors, the contribution of nerve sparing to early return of continence is supportive, and by 12 months postoperatively, healing and compensation by other mechanisms facilitate recovery. In expert hands, this impact may become minimal as surgeons develop several compensatory techniques that

Table 4 Autonomic nerve pathways to the US

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
1987	Kumagai, *Urol Res* [30]	Light microscopy + electron microscopy	?	Cystectomy specimen	Among the EUS cells, a large axon bundle is surrounded by perinerium; most axons are unmyelinated and each axon contains many small granular vesicles and larger granular vesicles which are considered to be adrenergic	Electron microscopy	Unmyelinated cholinergic axons were not recognized in the study; the adrenergic axon profile extended to the EUS itself and suggests a functional role as a sole mechanism of passive continence
1997	Hollabaugh, *Urology* [24]	Gross dissection	4	Adult bodies	After traveling deep in a groove along the rectum covered by the LAF, distinct branches of the IHP (pelvic nerve) connect to the EUS at the prostatic apex level, where they join the intrapelvic branches of the PuN and enter EUS at the 5 and 7 o'clock positions at the junction of the EUS and the LAM	Photographs	The IHP is located just at the tip of the SV and would be at risk for damage during dissection of the tips
2000	Strasser, *World J Urol* [21]	Gross dissection + 22 patients with ultrasound of the US	14	Adult bodies	The membranous urethra is innervated by branches derived from the prostatic plexus as well as the CNs and that run dorsolateral to the urethra to reach to periurethral connective tissue	Photographs	Most of the autonomic innervation of the remnant urethra should stay intact to ensure that both muscular resistance and relaxation are preserved postoperatively, despite the removal of a safe segment of the proximal urethra for oncological reasons
2003	Nelson, *J Urol* [31]	Intraoperative stimulation	8	Adult patients	Stimulation of the NVBs resulted in measurable and significant increases in intraurethral pressure	Urethral pressure	The finding of an intrapelvic urethral innervation supports the observation that nerve sparing RP may improve continence
2003	Akita, *Surg Radiol Anat* [16]	Gross dissection	44	Adult bodies	The lowermost branch of the PPx, from the caudal most branch of the PSN, ran on the rectal attachment of the LAM and reached the US muscle region	Photographs	It is important to preserve these branches during operations on the inferior rectal region
2005	Takenaka, *Urology* [26]	Gross dissection + histology	25	Adult bodies	Branches to the EUS arise from the NVB that leads to myelinated and unmyelinated branches to the EUS; at the apex, the nerves were located in the pararectal space on the dorsolateral side of the prostate passing through the rectourethral muscle with a tortuous course	LFB staining + histology	The rectourethral muscle should be incised near the apex to preserve the nerves passing through the muscle mass

Table 4 continued

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
2005	Karam, *Eur Urol* [25]	Histology	10	Fetuses	Most of the unmyelinated nerve fibers penetrate the US from the posterolateral surface; a majority of them approach the smooth muscular layers at 5 and 7 o'clock	LFB staining + CAAD	At risk of injury during dissection of the seminal vesicles and of the lateral aspects of the prostate
2007	Takenaka, *J Urol* [32]	Intraoperative stimulation	27	Adult patients	Electrostimulation of the NVB increases intracavernous and intraurethral pressure; the macroscopically identified NVB contained many nerve fibers not only to the cavernous tissue but also to the EUS and the bottom of the LAM	Urethral pressure	The surgically identified NVB contained some of the nerve fibers contributing to urinary continence
2008	Catarin, *J Urol* [27]	Postoperative stimulation	46	Adult patients	A significant increase in the urethro-anal reflex sensory threshold and latency was recorded, evidencing functional autonomic afferent denervation of the membranous urethra six months after RP	Urethro-anal reflex meas	Derangement in afferent autonomic innervation could affect the guarding reflex that automatically contracts the sphincter once a few drops of urine are in the membranous urethra
2010	Song, *Neurourol Urodyn* [20]	Gross dissection	15	Adult bodies	Pelvic nerves originate from the caudal most roots of the PSNs, run between the pelvic fascia and the LAM and terminate lateral to membranous urethra at the 5 and 7 o'clock positions; medial branches of the NVBs accompanying the membranous urethra pierce the urogenital diaphragm at the 3 and 9 o'clock positions	Photographs	Sympathetic nerves from S2 to S4 supply the smooth muscle sphincter; autonomic fibers are vulnerable to damage during seminal vesicle or apical dissection and may be implicated in recovery of urinary continence
2011	Alsaid, J Anat [17]	Histology	7	Fetuses	The NVB gave rise to nerve fibers following three major projections: to the US complex anteriorly, to the corpora cavernosa anterolaterally and to the corpus spongiosum posterolaterally	nNOS labeling + CAAD	The dual autonomic supralevator and somatic infralevator innervation occurred in five directions, playing a role in urination, defecation and sexual function, improving the understanding of the reflex loops around the LAM, and demonstrating the importance of autonomic nerve sparing during surgery

Table 4 continued

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
2014	Hinata, *Urology* [29]	Gross dissection + histology	14	Adult bodies	nNOS-positive nerves distributed along the superior aspect of the LAF in the levator hiatus, lateral to the EUS, and at the penile hilum immediately superior to the cavernous tissue; in all cadavers, nerves to the EUS originated from the CN at the inferomedial edge of the LAM slings and ran toward the penile hilum	Histology	Preservation of the NVB together with the LAF significantly improved early continence and sphincter fatigue symptoms after RARP
2015	Ganzer, *Eur Urol* [28]	Histology	5	Adult bodies	At the level of the EUS sphincter, 39 % of nerves shift to the dorsal region and some nerve fibers were even found scattering in the EUS muscle fibers.	Histology + planimetry	These dorsal nerves should be spared; angulated clamp should not be passed blindly under the urethra; only the dorsal raphe of the UES should be grasped if a posterior reconstruction (Rocco stitch) is performed

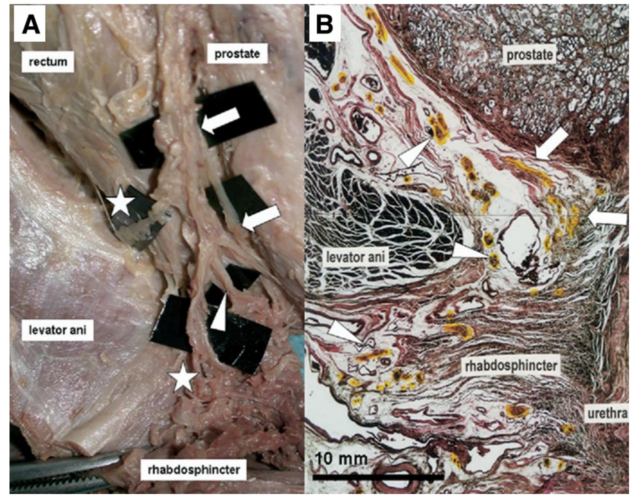

Fig. 5 Autonomic innervation. **a** Macroscopic dissection of so-called right NVB in fixed cadaver. NVB contains many nerve fibers to cavernous tissue (*arrowhead*), urethral sphincter (*arrow*) and bottom of levator ani muscle (*star*). **b** Frontal histological section around so-called right NVB stained with hematoxylin and eosin. Some nerve fibers go to cavernous tissues and urethral sphincter between membranous urethra and levator ani muscle fascia. H&E stain. Exact caption from the original article by Takenaka et al. [32] used with permission

may overcome the minimum neurological handicap that may occur due to nerve damage. We have summarized possible nerve routes to the sphincter that may help surgeons in visualizing their locations intraoperatively during radical prostatectomy (Fig. 2).

The possible locations of continence nerve injury are summarized in the flowchart that also discusses the possible mechanisms and strategies for avoidance even when performing non-nerve sparing surgeries (Fig. 10) [11, 13, 20, 38–42]. From the surgical technique standpoint, both somatic and autonomic nerves are at risk of damage, due to either wide excision at the level of the seminal vesicles or the peri-prostatic dissection, or at the level of the apex where convergence occurs and the nerves are within a few millimeters of the dissection plane and suture bites. The somatic and autonomic nerves travel within the layers of FLA and could sustain injury if the resection plane is sufficiently wide. Visualizing the existence and course of these nerves may help surgeons minimize the damage to these potentially important structures. These nerves could be damaged not only by surgical excision but also by cautery, clips or sutures that are used to control bleeding.

Conclusion

It is important to understand the complex innervation of the US such that incontinence associated with radical

Table 5 Nerve communications supplying innervation to the US

Year	References	Methodology	*N*	Material	Anatomical facts	Evidence	Discussion
1997	Hollabaugh, *Urology* [24]	Gross dissection	4	Adult bodies	The pelvic nerve is joined by an intrapelvic branch of the PuN, under the LAF and at the level of prostatic apex	Photographs	Vesicourethral anastomotic sutures should avoid the 5 and 7 o'clock areas and should only include the 3- to 5-mm edge of the urethra to avoid snaring the somatic and autonomic innervation of the EUS
2010	Song, *Neurourol Urodyn* [20]	Gross dissection	15	Adult bodies	Communicating branches between the PuN, LAN and PSN were identified in 67 % of specimens; the PSN and LAN originated from the same nerve trunk	Photographs	Intralevatorian nervous communications may determine an important role of the LAM in maintaining continence
2003	Akita, *Surg Radiol Anat* [16]	Gross dissection	44	Adult bodies	The root of the caudal most branch of the PSN frequently (94 %) formed a common trunk with the LAN; other inconstant small twig fusions observed: branch from PuN with branch to the rhabdosphincter (20 %), branch of the LAN with the PuN (30 %) or with branch to the region from the PPx (10 %)	Photographs	In many branches of the PPx, communications were found only with the branches to the urethral sphincter muscle region
2005	Takenaka, *Urology* [26]	Gross dissection + histology	25	Adult bodies	1–3 Communications between the intrapelvic and extrapelvic nerves (inconstant, 40 %)	Histology	The intrapelvic nerves generally ran in a ventral-inferior-medial direction along the covering LAF, but detailed topographical information could not be obtained
2011	Alsaid, *J Anat* [17]	Histology	7	Fetuses	3 levels of connections between the supralevator-autonomic and the infralevator-somatic pathways: proximal (somatic, from the origin of the PuN to the lateral or posterior branches of the IHP), intermediate (autonomic, inconstant 29 %, lateral fibers of the IHP through the LAM, few of them reaching the PuN) and distal (autonomic nitrergic, at the hilum of the penis between the NVB and the DPN)	PMP22 and nNOS labelings + CAAD	These autonomic–somatic communicating branches suggests possible nervous plasticity of potential clinical interest for the prevention or treatment of postoperative urogenital and digestive dysfunctions

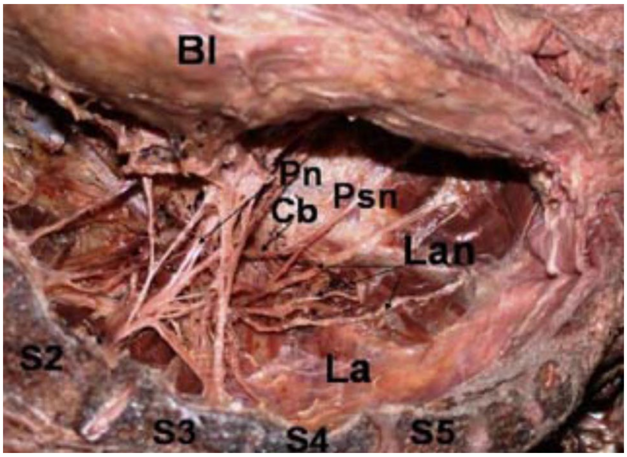

Fig. 6 Somatic–autonomic communications. Communicating branches between pudendal nerve, pelvic splanchnic nerves and nerves to the levator ani nerve (*left*). *Bl* bladder, *La* levator ani, *Lan* levator ani nerve, *Psn* pelvic splanchnic nerves, *Cb* communicating branches. Exact caption from the original article by Song et al. [20] used with permission

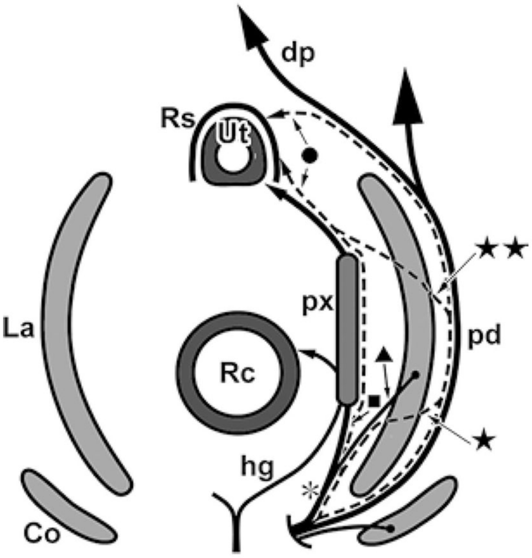

Fig. 8 Schematic presentation of the positional relationship between the nervous branches to the rhabdosphincter (*black dot*) and the levator ani. The somatic nervous branches to the rhabdosphincter might have two routes to reach the muscle (*dashed line*): one is a course from the pudendal nerve, and the other from the pelvic plexus. The pelvic splanchnic nerve (*black square*) forms a common trunk (*asterisk*) with the nerve to the levator ani (*black triangle*). A connecting branch between the nerve to the levator ani and the pudendal nerve (*black star*) and a connecting branch between the pudendal nerve and the branch to the rhabdosphincter from the pelvic plexus (*double black stars*) are sometimes observed. *Co* coccygeus, *dp* dorsal nerve of the penis, *hg* hypogastric nerve, *La* levator ani, *pd* pudendal nerve, *px* pelvic plexus, *Rc* rectum, *Rs* rhabdosphincter, *Ut* urethra. Exact caption from the original article by Akita et al. [16] used with permission

prostate cancer surgery can be minimized. It appears that the complexity of the neuroanatomy of the US include significant cross-communication, redundancy and possibly neuroplasticity. It seems that both somatic and autonomic systems contribute to the innervation, and pelvic surgery poses risks to the integrity of many of these nerves. The autonomic nerves travel with the neurovascular bundles or travel separately or as communication with somatic nerves. The somatic nerves are shown to

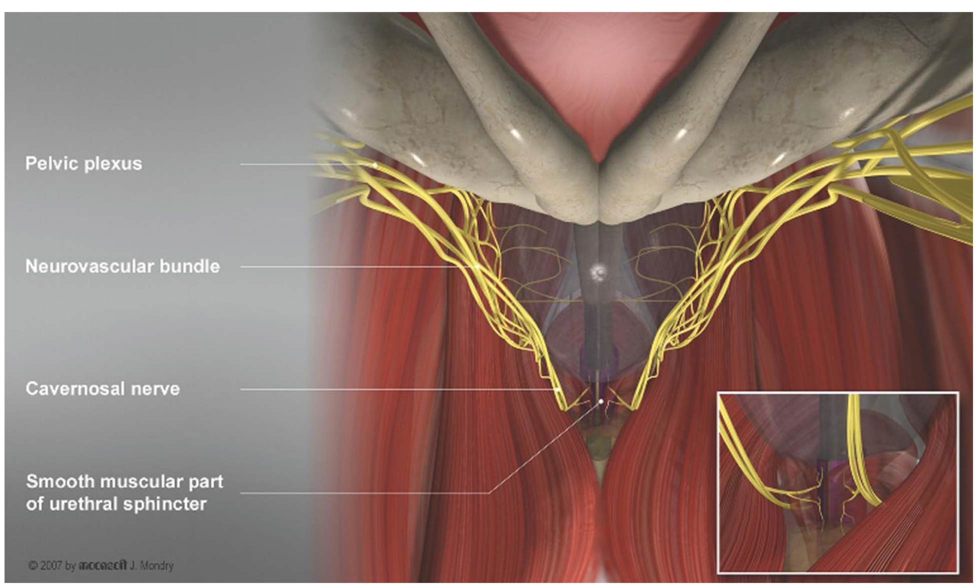

Fig. 7 Autonomic nerves branching from cavernosal nerves to the urethra (3D visualization). The cavernosal nerves of the penis emerge from the neurovascular bundles and divide into medial and lateral branches after penetration of the muscular pelvis. The medial branches innervate smooth muscle component of the external urethral sphincter; the lateral branches continue to enter the cavernosal bodies. Exact caption from the book chapter by Schwalenberg et al. [36] (book by Stolzenburg et al.) used with permission

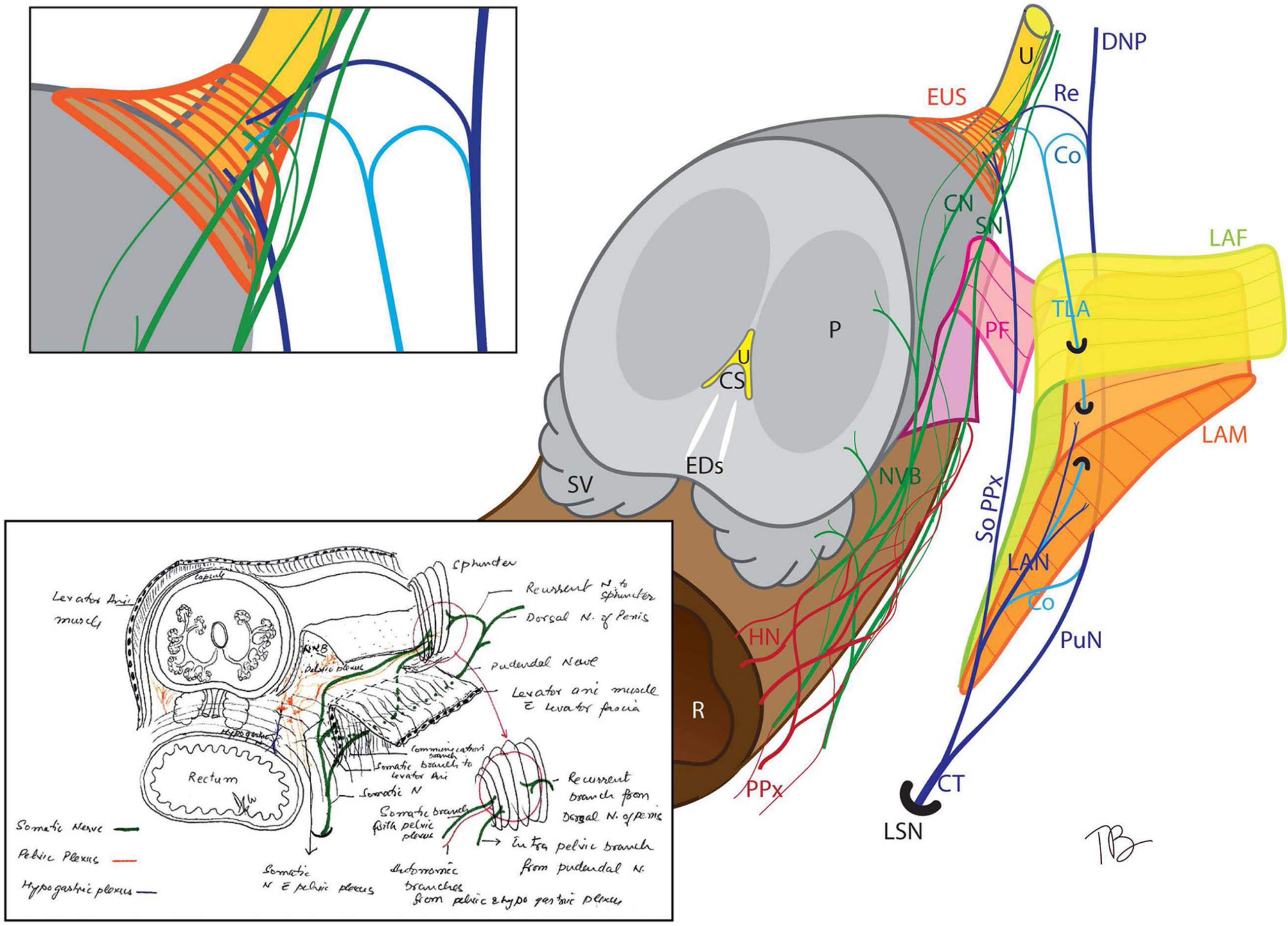

Fig. 9 Integrated representation of the possible US innervation pathways. Surgeon's (AKT) conception (*bottom left frame*) with anatomical (TB) reproduction. Somatic pathway in *dark blue*; neurovascular bundle in *green*; pelvic plexus in *red*; communications in *light blue*. *Co* communicating branches, *CN* cavernous nerve, *CS*, colliculus seminale, *CT* common trunk of the LAN and PuN, *DNP* dorsal nerve of the penis, *EDs* ejaculatory ducts, *EUS* external urethral sphincter, *HN* hypogastric nerve, *LAF* fascia of levator ani, *LAM* levator ani muscle, *LAN* levator ani nerve, *NVB* neurovascular bundle, *P* prostate, *PF* pelvic fascia, *PPx* pelvic plexus, *PuN* pudendal nerve, *Re* recurrent branches of the DNP, *SoPPx* somatic pelvic plexus, *SN* spongious nerves, *LSN* lesser sciatic notch, *SV* seminal vesicle, *TLA* trans-levator ani branch, *U* urethra

Table 6 Level of evidence of the nerve pathways to the US

0	+	++	+++	++++	+++++
No data	Low	Medium-low	Medium-high	High	Certainty

	Quantity of studies and anatomical subjects	Dissection and illustrations	Histology	Electronic microscopy	Electrophy siology	Overall estimated certainty
Somatic pudendal extrapelvic	++++	+++++	+++++	0	+++++	++++
Somatic pudendal intrapelvic	+++	++++	+	0	0	++
Somatic extrapudendal intrapelvic	+++	+	+	0	++	+
Autonomic	+++++	++++	++++	++	+++	++++
Communications	++++	++++	++++	0	0	+++

For each of the described pathways, the different types of anatomical evidence available in all the studies have reviewed, evaluated and then reported in a subjective gray-scale table (weight = no anatomical facts available; dark = strong estimated certainty). The last column summarizes the authors' level of certainty for each pathway after reviewing all of the anatomical data

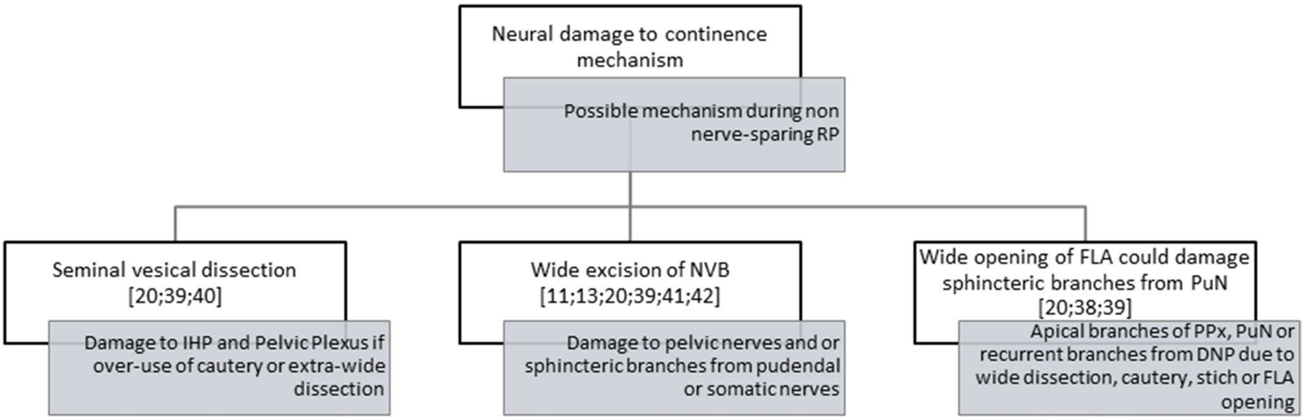

Fig. 10 Technical refinements in nerve sparing to avoid incontinence

come from both pudendal and non-pudendal pathways. Specifically, nerves can get damaged at higher levels, during seminal vesicle dissection, or at lower levels, during periprostatic and apical dissections. Research that continues to elucidate the neuroanatomy of the US will enable surgeons to avoid destruction of these important structures and thereby minimize the incontinence associated with pelvic surgeries.

Authors' contribution T. Bessede contributed to data selection, data analysis, writing and drawing. P. Sooriakumaran and A. Takenaka participated in project development and significant revisions. A. Tewari was involved in project development, data selection and writing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards This article does not contain any studies with human participants or animals performed by any of the authors.

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