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Anatomical grades of nerve sparing: a risk-stratified approach to neural-hammock sparing during robot-assisted radical prostatectomy (RARP)

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Accepted for publication 22 July 2011

OBJECTIVES

- To report the potency and oncological outcomes of patients undergoing robot-assisted radical prostatectomy (RARP) using a risk-stratified approach based on layers of periprostatic fascial dissection.
- We also describe the surgical technique of complete hammock preservation or nerve sparing grade 1.

PATIENTS AND METHODS

- This is a retrospective study of 2317 patients who had robotic prostatectomy by a single surgeon at a single institution between January 2005 and June 2010.
- Included patients were those with ≥1 year of follow-up and who were potent preoperatively, defined as having a sexual health inventory for men (SHIM) questionnaire score of >21; thus, the final number of patients in the study cohort was 1263.
- Patients were categorized pre-operatively by a risk-stratified approach into risk grades 1–4, where risk grade 1 patients received nerve-sparing grade 1 or complete hammock preservation and so on for risk grades 2–4, as long as intraoperative findings permitted the planned nerve sparing.
- We considered return to sexual function post-operatively by two criteria: i) ability to have successful intercourse (score of ≥4 on question 2 of the SHIM) and ii) SHIM >21 or return to baseline sexual function.

What's known on the subject? and What does the study add?

During radical prostatectomy, urological surgeons have tried to identify the "cord-like NVB" at the lateral aspect of the prostate. However, little histological or physiological investigation was conducted to verify that the NVB identified at surgery really included the cavernous nerve. Recently, there have been observations that refute the dogma that the cavernous nerve is always within the NVB.

In this study, we have described a hammock-like distribution of the nerves on which the prostate rests, demonstrating that the NVB is more a network of multiple fine dispersed nerves than a distinct structure. We presented a novel nerve-sparing approach to complete hammock preservation. This risk-stratified approach for determining the degree of nerve sparing based on the patient's likelihood of ipsilateral EPE seeks to categorize patients for optimal balance between oncological outcomes and functional outcomes.

RESULTS

- There was a significant difference across different NS grades in terms of the percentages of patients who had intercourse and returned to baseline sexual function ($P < 0.001$), with those that underwent NS grade 1 having the highest rates (90.9% and 81.7%) as compared to NS grades 2 (81.4% and74.3%), 3 (73.5% and 66.1%), and 4 (62% and 54.5%).
- The overall positive surgical margin (PSM) rates for patients with NS grades 1, 2, 3, and 4 were 9.9%, 8.1%, 7.2%, and 8.7%, respectively ($P = 0.636$).
- The extraprostatic extension rates were 11.6%, 14.3%, 29.3%, and 36.2%, respectively ($P < 0.001$).
- Similarly, in patients younger than 60, intercourse and return to baseline sexual function rates were 94.9% and 84.3% for NS grade 1 as compared to 85.5% and 77.2% for NS grades 2, 76.9% and 69% for NS grades 3, and 64.8% and 57.7% for NS Grade 4 ($P < 0.001$).

CONCLUSIONS

- The risk-stratified approach and anatomical technique of neural-hammock sparing described in the present manuscript was effective in improving potency outcomes of patients without compromising cancer control.
- Patients with greater degrees of NS had higher rates of intercourse and return to baseline sexual function without an increase in PSM rates.

KEYWORDS

erectile dysfunction, prostate cancer, nerve sparing, robotic prostatectomy, neural hammock

FIG. 1. Description of the cohort. ED, erectile dysfunction.

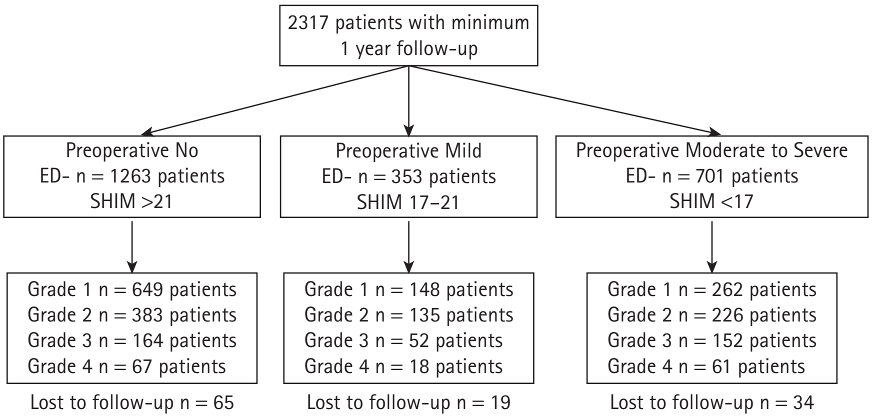
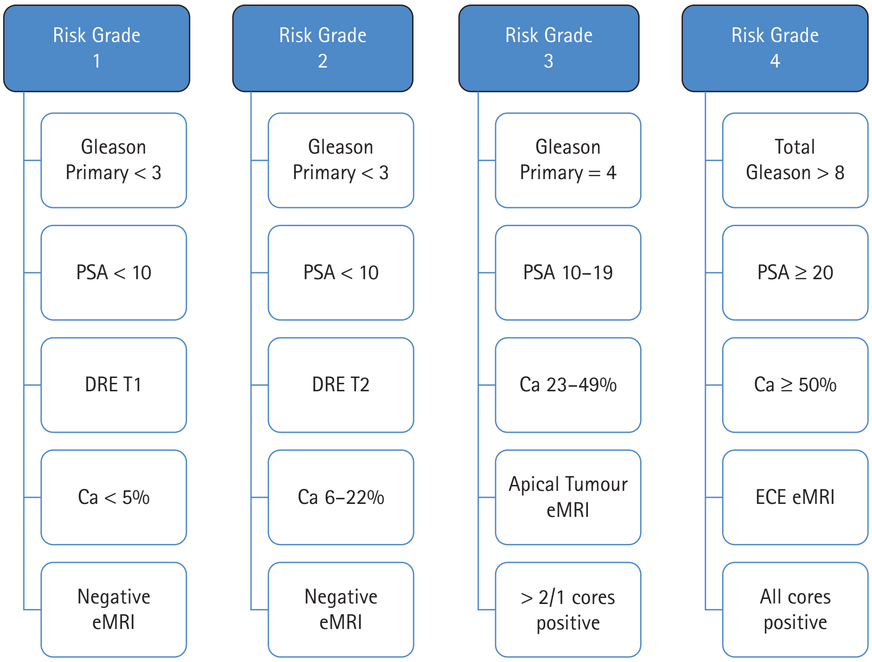


FIG. 2. Cornell algorithm for risk-stratified approach to NS. PSA levels in ng/mL. Ca, Maximum % cancer in any biopsy core.



INTRODUCTION

Sexual dysfunction after radical prostatectomy (RP) still remains an enigma, even after the original description of the neural pathways by Walsh and Donker [1] in 1982. Despite advances in technique and surgical technologies, the percentage of patients that have a return of erectile function sufficient for sexual intercourse 1 year after surgery varies from 15% to 87% in contemporary RP series [2–4]. Data from the Prostate Cancer Outcomes Study suggest that sexual dysfunction after RP has a significant impact on health-related quality of life (HRQL) for men, affecting everyday interactions with partners and their own perceptions of their sexuality; this is especially the case for younger men [5,6]. New studies have been helpful in explaining variations in the neurovascular bundles (NVBs), accessory neural pathways, trizonal neural architecture, neural hammock, orgasmic nerves, and periprostatic nerve compartments [7,8], which could significantly alter potency outcomes.

In the present manuscript, we summarise the neuroanatomical findings upon which we have developed our anatomical robotic technique and discuss our risk-stratified approach to nerve sparing (NS), which gives more patients the opportunity to undergo NS while achieving cancer control by maintaining excellent surgical margin rates. We then present the patient-reported sexual outcomes of 2317 consecutive patients (January 2005 to June 2010) who had ≥1 year of follow-up and were operated on by one surgeon (A.K.T.) at a single institution.

PATIENTS AND METHODS

STUDY COHORT

This is a retrospective study of 2317 patients who had robot-assisted RP (RARP) by one surgeon (A.K.T.) at a single institution between January 2005 and June 2010. Included patients were those with ≥1 year of follow-up and who were potent preoperatively, defined as having a sexual health inventory for men (SHIM) questionnaire score of >21; thus, the final number of patients in the study cohort was 1263 (Fig. 1). Patients were categorized preoperatively by a risk-stratified approach into risk grades 1–4, where risk grade 1 patients received NS grade 1 and so on for risk grades 2–4 (with NS grade 4 being non-NS), as long as intraoperative findings permitted the planned NS (Fig. 2). Note that the current classifications for NS grades were only finalised and applied to patients preoperatively starting in December 2008; for previous surgeries, intraoperative videos were reviewed by the lead surgeon (A.K.T.) and a member of the research team (A.S.) to assign standardised grades of NS for the purposes of the present study.

DATA COLLECTION

Data for baseline variables such as age, PSA level, height, weight, co-morbidities, biopsy information, and sexual outcomes were collected under an Institutional Review Board-approved protocol concerning HRQL in patients undergoing RARP at our institution. The baseline sexual outcomes were collected using a patient-reported, validated HRQL instrument, the SHIM.

PATIENT FOLLOW-UP

SHIM questionnaires were dispatched to patients via postal or electronic mail at 6, 12, 26, and 52 weeks after RARP. A member of the research team then contacted subjects via telephone at each of the above follow-up intervals to ensure receipt of the questionnaire. A third party (not involved in patient care) performed data collection and follow-up correspondence in compliance with the Health Insurance Portability and Accountability Act.

We considered return to sexual function postoperatively by two criteria: (i) ability to have successful intercourse (score of ≥4 on question 2 of the SHIM) and (ii) a SHIM score of >21 or return to baseline sexual function. Penile rehabilitation was recommended for all patients; patients were advised to use phosphodiesterase type 5 inhibitors at least three times per week until return of sexual function. If patients required vacuum erectile devices, penile injections, or transurethral alprostadil for intercourse, they were not considered to have fulfilled the above criteria for potency. The returned responses to the outcomes questionnaires, together with the patients' preoperative, intraoperative, and postoperative clinicopathological data, were prospectively entered into a password-protected Microsoft® Access database.

STATISTICAL METHODS

Statistical analysis was performed using PASW version 18.0 (SPSS, Inc., Chicago, IL, USA), with $P < 0.05$ considered to indicate statistical significance. Chi-square tests were used to compare sexual function outcomes, positive surgical margin (PSM) rates, and extraprostatic extension (EPE) rates of NS grades 1–4.

PATHOLOGICAL DATA COLLECTION

Dedicated genitourinary pathologists in our institution examined the pathological specimens (M.M.S., B.D.R.). Our specimen handling protocol has been published previously, where we described our fresh tissue banking protocol [9]. The genitourinary pathologists worked closely with the surgical team in ensuring safe tissue banking and meaningful clinical interpretation. The surgical and pathological teams routinely reviewed the preoperative histopathology, endorectal MRI (eMRI) data, and intraoperative videos for meaningful correlations between eMRI data, intraoperative findings, and histopathological slides. The genitourinary pathologists summarized the final pathological staging and margin status in a standardized synoptic report after reviewing the whole specimen, deeper sections, tissue-banking specimens, surgical videos, and intraoperative biopsies, when necessary. The tissue-banking specimens were only released when clinical reporting had concluded [9].

SURGICAL TECHNIQUE

ATHERMAL, TRACTION-FREE, AND RISK-STRATIFIED APPROACH TO PRESERVATION OF NEURAL HAMMOCK DURING RARP

Our technique is based on recent anatomical data, incorporating delicate tissue handling strategies as guided by penile tissue monitoring studies [10]. The technique is anatomical, trizonal, traction-free, athermal, and risk-stratified. It avoids/minimizes periprostatic dissection and manipulation, attempts to preserve the neural hammock, and bases dissection on the guidance of visual cues.

A) TECHNICAL STEPS FOR NS

Our technique of transperitoneal RARP has been described previously [10–12]. Presented herein is the synopsis of our NS approach. To begin, the anterior surface of the bladder and prostate is exposed, the endopelvic fascia is minimally incised, and the bladder neck is entered in the midline. The catheter is gently retracted to expose and deliver the vasa deferentia and seminal vesicles more anteriorly. Using sharp scissors and curved forceps, we separate the capillaries and veins from the underlying vasa deferentia and seminal vesicles, clipping when appropriate. The cut ends of the vasa deferentia are pulled to further expose the seminal vesicles. The seminal vesicles are encased in their own fascial compartment and most of the vessels and nerves travel or enter at the tip or lateral aspect. Therefore, the medial avascular compartment is a logical entry point to start the intrafascial dissection during a NS procedure. The medial avascular plane is slowly developed, and the seminal vesicles are exposed anteromedially. Care is taken in the lateral dissection by minimizing the traction and using small pedicle clipping to preserve delicate proximal neurovascular plate and hypogastric branches.

B) INSIDE-OUT APPROACH FOR NEURAL HAMMOCK PRESERVATION

Next, both seminal vesicles and vasa deferentia are lifted up. Denonvilliers' fascia is tented and entered in the midline by sharp incision. Based on the preoperative oncological parameters, a decision about the type of NS is made and the appropriate fascial plane within the layers of Denonvilliers' fascia is entered, so as to gently develop the retroprostatic space. The individual small arterial and venous bleeders are either controlled cut or cold cut based on intraoperative judgment. The retroprostatic space is first extended distally to expose the under-surface of the prostato-urethral junction. Dissection of this plane is slowly carried out laterally on the side with oncologically less aggressive cancer. By now, we have freed up the predominant NVB (PNVB) from the posterolateral aspect of the prostate. Further dissection actually creates a plane between the neurovascular hammock and the lateral aspect of the prostate. This plane is easier to develop distally because there are fewer perforating vessels into the gland. These perforating vessels are identified and sharply cut. Some of them require clipping, and most stop bleeding in a few seconds. A similar plane is developed on the contralateral side to release the entire posterior aspect of the hammock. So far, we have not applied any traction to the hammock, and at this time the hammock is only attached to the prostate at the base where large branches of the inferior vesicular artery form the pedicle and enter the prostate and seminal vesicle base. The hammock is also adhered to the prostate bilaterally at the anterolateral edge where fascial compartments fuse with the endopelvic fascia and anterior fibromuscular stroma of the prostate. This early release of the hammock posteriorly actually minimizes the traction on the neural tissue and better defines the pedicle. The pedicle has two distinct components, a medial one that

FIG. 3. Histology of non-NS RP specimen with wide excision of adjacent tissue. Note the distribution of nerve fibres (highlighted in green) in the periprostatic fascial layers. The collapsible veins on the prostate capsule (outlined in blue) are a distinct anatomical landmark – most of the periprostatic nerve fibres lie lateral to these veins. Notice also the area of EPE of cancer through the prostate capsule adjacent to these veins. N, nerve.

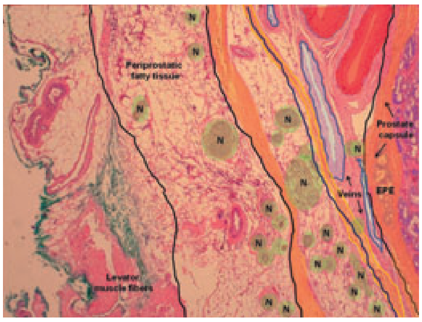
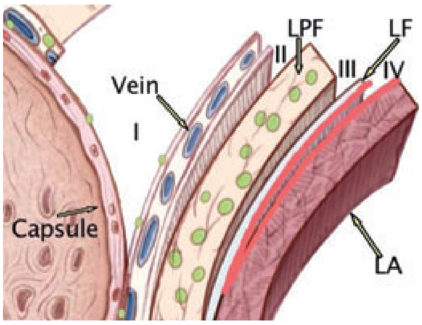


FIG. 4. Layers of fascia enveloping the prostatic capsule, showing the planes of dissection for differing NS grades (1–4). LPF, lateral pelvic fascia medial layer, i.e. the prostatic fascia; LF, lateral pelvic fascia lateral layer, i.e. the levator fascia; LA, levator ani.



enters the base of the seminal vesicle and the medial aspect of the prostatic base, and a more lateral one that contains larger vessels entering the posterolateral and anterolateral corners of the prostatic base. The neurovascular hammock is intermingled with these two components of the pedicle; it has already been separated by our approach of midline entry into the periprostatic plane and gentle release from medial to lateral and then anterior aspect of the prostate. The medial pedicle is controlled using one to three small 5-mm clips and sharply cut. Sharp dissection is important because it avoids traction on the nerves, inadvertent development of tissue flaps, and iatrogenic positive margins ("intraprostatic incision"). However, sharp dissection requires appreciation of appropriate surgical planes and exploitation of visual cues to recognise various structures and pathologies (inflammation, EPE, etc.). Next, the lateral pedicle is similarly controlled and cut in small parts. Once the entire pedicle is cut, the rest of the hammock is easily released, and the anterolateral edge is either clipped or controlled using a 4-0 suture to minimize bleeding from the anterolateral edge of the hammock, which mostly consists of periprostatic veins. We often see an anterolateral arterial trunk that travels from proximal to distal and disappears in the pelvic floor, possibly to supply the urethra or penis. Special attempt is made in separating this artery from the prostatic pedicle to which it is intimately attached. Preservation of this and additional arterial trunks maximizes the viability of neurovascular tissue, as some of them may be vasa nervora or provide significant arterial supply to the cavernosal tissue. Traction on these vessels could actually produce distal ischaemic changes as noted in our penile oxygenation studies [10].

Next, attention is directed to the distal aspect of the anterolateral edge of the hammock, which is released under vision starting from the prostatic apex. The prostate is lifted up, and, using the 30 ° lens facing upward, we release the distal 1 cm of the hammock, taking care to avoid any traction or blunt dissection. This is the final common pathway of the pelvic nerves while they are exiting the pelvis. There are one or two peri-apical arteries that are controlled and cut. The retro-apical plexus (part of the distal hammock) is left untouched and dropped posteriorly. The urethro-prostatic junction is transected, and the freed prostate is packed in the EndoCatch™ bag. The surgical field is inspected for significant bleeding; the bleeders are either clipped or sutured using a figure-of-eight suture. If there is a need for retracting the hammock during NS, we use 4-0 sutures to minimize tissue trauma and traction.

Next, lymph node dissection is performed, followed by vesico-urethral anastomosis and total anatomical reconstruction. During reconstruction, we especially pay attention to the location of the retro-apical plexus and thus avoid its inadvertent inclusion in the suture. The procedure is completed after placing a drain.

C) BALANCING NERVE PRESERVATION WITH CANCER CONTROL: A RISK-STRATIFIED APPROACH

Striving to balance the competing goals of cancer clearance with preservation of potency, a risk-stratified approach toward NS according to the patient's likelihood of ipsilateral EPE has been adopted at our institution. The patient's PSA level, biopsy Gleason score, percentage of cancer in the biopsy, number of positive cores, presence of unilateral vs bilateral positive cores (used as a surrogate for high-volume cancer or multifocality), clinical stage, findings of the eMRI for cancer localization, tumour volume, presence or absence of EPE, and status of periprostatic tissue are parameters that are used to select patients for NS RP. Our approach to NS during RARP involves varying degrees of preservation of the nerve fibres in the various fascial planes (Figs 3–5). We refer to them as:

- Grade 1 NS – Incision of the Denonvilliers' and lateral pelvic fascia (LPF) is taken just outside the prostatic capsule. We also describe this as medial venous plane for complete hammock preservation. This represents the greatest degree of NS possible, and we perform this procedure only for patients with no-to-minimal risk of EPE.
- Grade 2 NS – Incision through the Denonvilliers' (leaving deeper layers on the rectum) and LPF is taken just outside the layer of veins of the prostate capsule. We also describe this as peri-venous plane of hammock preservation. This preserves most large neural trunks and ganglia and is used for patients at low risk of EPE.
- Grade 3 (partial/incremental) NS – Incision is taken through the outer compartment of the LPF (leaving some yellow adipose and neural tissue on the specimen), excising all layers of Denonvilliers' fascia. This is performed for patients with moderate risk of EPE because some of the medial trunks are sacrificed, while the lateral trunks are preserved.
- Grade 4 (non-NS) NS – These patients have high risk of EPE and are not candidates for NS. Here, we perform a wide excision of the LPF and Denonvilliers' fascia containing most of the periprostatic neurovascular tissue. In selected patients, we attempt nerve advancement of the identifiable ends of the NVBs.

FIG. 5. eMRI images, intraoperative view, gross specimen and correlation from haematoxylin and eosin (H&E)-based anatomy of (a) Grade 1 NS, (b) Grade 2 NS, (c) Grade 3 NS, and (d) Grade 4 NS (non-NS).

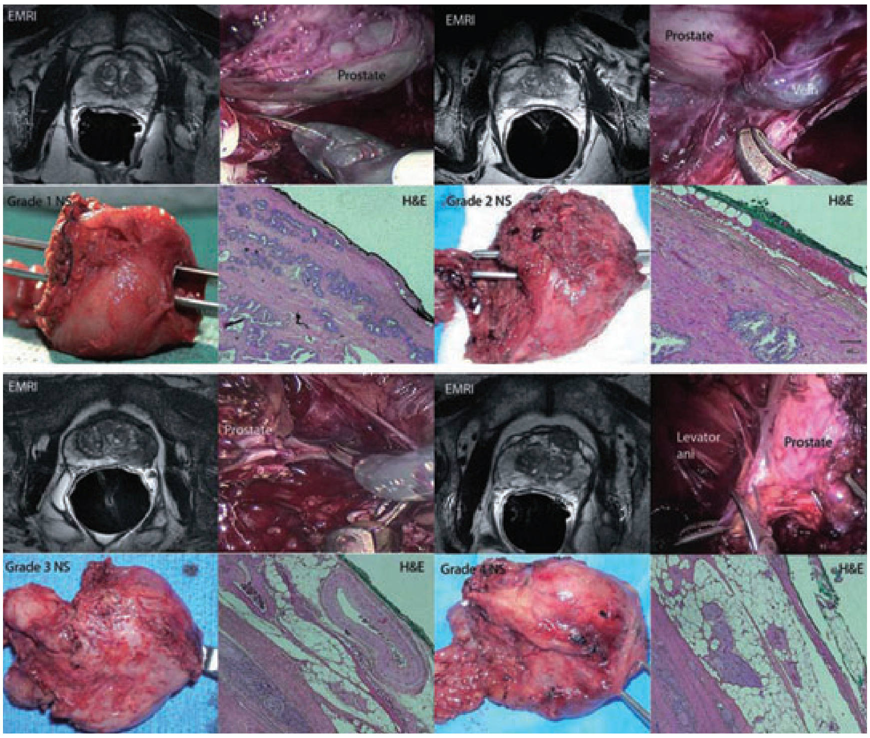


TABLE 1 Baseline demographics, clinical, pathological and biochemical recurrence data of 1263 patients who had ≥1 year follow-up

Variable	Value
Total number of patients	1263
Median (interquartile range):	
Age, years	58 (53, 63)
Body mass index, kg/m^2	26 (24, 29)
Preoperative PSA level, ng/mL	4.7 (3.6, 6.3)
Preoperative SHIM	25 (23.6, 25)
Prostate volume, mL	45 (37, 55)
%:	
Clinical stage:	
T1	84.9
T2	14.8
T3	0.3
Biopsy Gleason:	
≤6	59.3
7 (3 + 4)	25.4
7 (4 + 3)	9.2
≥8	6.1
Pathology Gleason:	
≤6	30.2
7 (3 + 4)	49.6
7 (4 + 3)	15.1
≥8	5.1
Pathology stage:	
T2	83.9
T3	16.1
Lymph-node positive	0.3
PSM	9.0
Biochemical recurrence	4.1

FIG. 6. Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21 with ≥1 year follow-up (n = 1198).

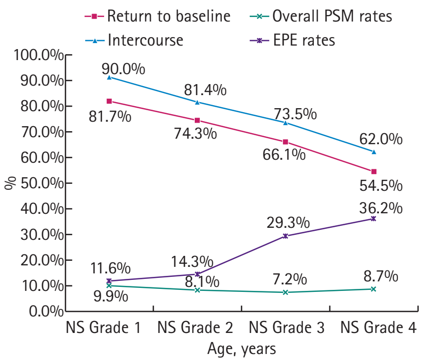
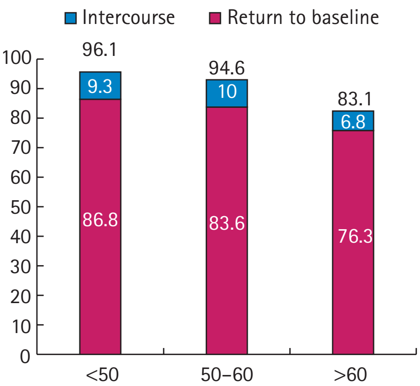


FIG. 7. Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21, NS Grade 1 with ≥1 year follow-up and categorized by their age (n = 619).



Note that patients with different NS grades on each side of the prostate are classified according to the higher NS grade of the two in the present study.

RESULTS

In all, 1263 patients with no preoperative erectile dysfunction were selected for the present study, and their baseline demographics, clinical data, pathological data, and biochemical recurrence rates are summarized in Table 1. In all, 65 patients were lost to follow-up in this group, and therefore potency outcomes were available in 1198 patients.

There was a significant difference across different NS grades for the percentages of patients who had intercourse and returned to baseline sexual function ($P < 0.001$), with those that underwent grade 1 NS having the highest rates (90.9% and 81.7%) as compared with NS grades 2 (81.4% and 74.3%), 3 (73.5% and 66.1%), and 4 (62% and 54.5%) (Table 2, Fig. 6).

The overall PSM rates for patients with NS grades 1, 2, 3, and 4 were 9.9%, 8.1%, 7.2%, and 8.7%, respectively ($P = 0.636$); the EPE rates were 11.6%, 14.3%, 29.3%, and 36.2%, respectively ($P < 0.001$).

There were also significant differences in the percentages of patients who had intercourse and returned to baseline sexual function across patients with no preoperative ED in different age groups ($P < 0.001$), as shown in Fig. 7. The percentages of patients who had intercourse and were aged <50, 50–60,

TABLE 2 Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21 with ≥1 year follow-up (n = 1198)

Variable	NS grade 1	2	3	4	*P*
N	619	363	154	62	
%:					
Intercourse	90.9	81.4	73.5	62	<0.001
Return to baseline (SHIM > 21)	81.7	74.3	66.1	54.5	<0.001
Overall PSM rates	9.9	8.1	7.2	8.7	0.636
EPE rates	11.6	14.3	29.3	36.2	<0.001

TABLE 3 Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21, aged ≤60 years with ≥1 year follow-up (n = 762)

Variable	NS grade 1	2	3	4	*P*
N	412	231	82	37	
%:					
Intercourse	94.9	85.5	76.9	64.8	<0.001
Return to baseline (SHIM > 21)	84.3	77.2	69	57.5	<0.001
Overall PSM rates	9.5	7.1	6.7	10	0.665
EPE rates	9	13.4	25.6	30	<0.001

and >60 years were 96.1%, 94.6%, and 83.1%, respectively. The rates of return to baseline sexual function were 86.8%, 83.6%, and 76.3%, respectively.

When only the patients that were aged <60 years were considered, there were the same general trends as seen in Table 2 (Table 3, Fig. 8). The percentages of patients that had intercourse with NS grades 1, 2, 3, and 4 were 94.9% 85.5%, 76.9%, and 64.8%, respectively ($P < 0.001$), while the percentages of patients who had a return to baseline sexual function were 84.3%, 77.2%, 69%, and 57.5%, respectively ($P < 0.001$). The overall PSM rates were 9.4%, 7.1%, 6.7%, and 10%, respectively ($P = 0.665$); the EPE rates were 9%, 13.4%, 25.6%, and 30%, respectively ($P < 0.001$). The rates of intercourse and return to baseline sexual function at 6, 12, 26, and 52 weeks for NS grade 1 patients who were aged ≤60 years are shown in Fig. 9, and comparisons of the preoperative and postoperative SHIM scores of each individual patient in this group are presented in the radar chart in Fig. 10.

DISCUSSION

Much of the progress achieved in the past two decades in improving potency outcomes after RP has resulted from an increased appreciation of the anatomical basis of the nerves responsible for erection.

The autonomic nervous system is directly responsible for penile erection. The inferior hypogastric (pelvic) plexus (IHP) is responsible for the mechanisms of erection, ejaculation, and urinary continence. The IHP contains sympathetic and parasympathetic components: the sympathetic fibres arise from the T11–L2 ganglia, while the parasympathetic fibres originate from the ventral rami of S2, S3 and S4. The IHP is a dense network of neural fibres located within a fibro-fatty, sub-peritoneal plate between the urinary bladder and rectum [13].

In 1982, Walsh and Donker [1] first published their seminal study detailing the anatomy of the nerves supplying the corpora cavernosa in male stillborns. Subsequent cadaveric and intraoperative studies by Walsh and colleagues [14,15] further elucidated that the NVBs run posterolateral to the prostate between two layers of LPF, the prostatic fascia medially and levator fascia laterally. Most of the cavernosal nerve fibres, ≈6 mm wide, then run caudally at the 3 and 9 o'clock positions of the membranous urethra beneath the striated external urethral sphincter at the prostatic apex.

FIG. 8. Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21, aged ≤60 years with ≥1 year follow-up (n = 762).

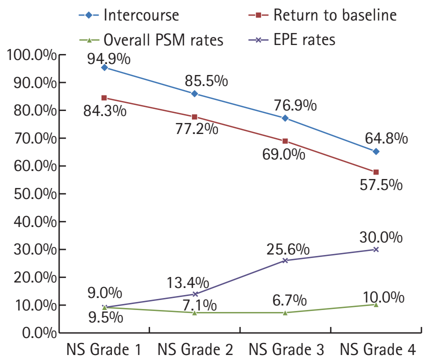
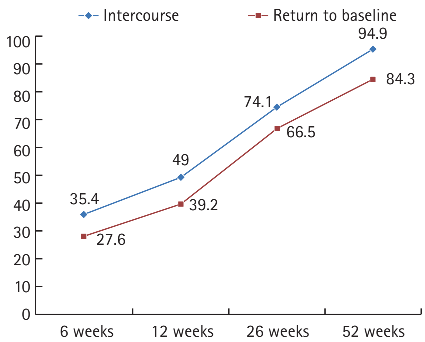


FIG. 9. Potency outcomes in patients with no erectile dysfunction preoperatively and SHIM scores of >21, aged ≤60 years, who underwent NS grade 1 with ≥ year follow-up, at each of the follow-up intervals (n = 412).



More recent studies suggest that the course of the NVBs is more complex than previously described by Walsh. In 2003, Tewari *et al.* [7] noted that there are several smaller nerves, which ramify in the periprostatic space and in the Denonvilliers' fascia. The exact physiological role of these smaller nerves in erection is not well defined (Fig. 11), but it is possible that they contribute to the neural impulses to the cavernosal tissue. In 2004, Costello *et al.* [8] showed in cadaveric dissections that the NVBs, although hard to distinguish, descend posteriorly to the seminal vesicles, converging at the mid-prostatic level and then diverging again when approaching the prostatic apex. Our group has described a

FIG. 10. *Radar chart showing comparisons of the preoperative and postoperative SHIM scores of each individual patient with SHIM scores of >21, aged ≤60 years and NS grade 1 (n = 412). Blue plot indicates the preoperative SHIM scores and pink plot indicates the postoperative SHIM scores of the patients. Orange circle marks the boundary of SHIM score of 22 and green circle marks the boundary of SHIM score of 17. The extent of blue areas correlates with postoperative loss of potency. Each line inside the circle in the radar chart represents a person. The patients are sorted by their preoperative SHIM scores in this radar chart.*

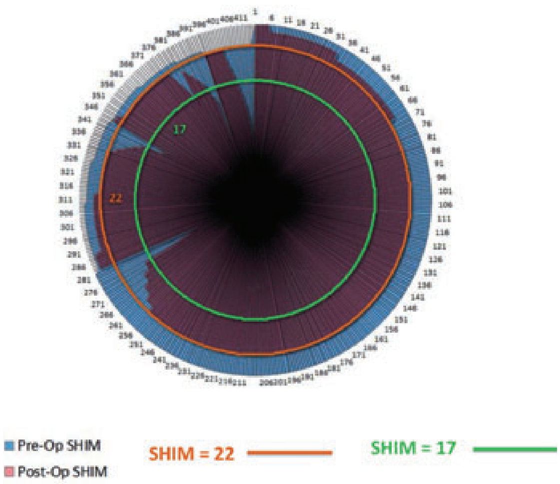


FIG. 11. *Left side of apex showing delicate nature of the NVB, nerve plexus and cross communications.*

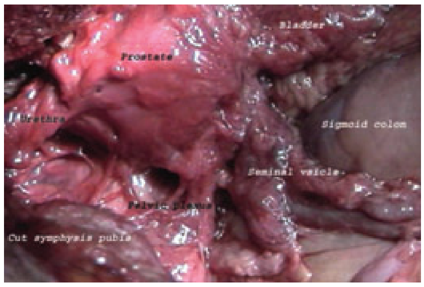
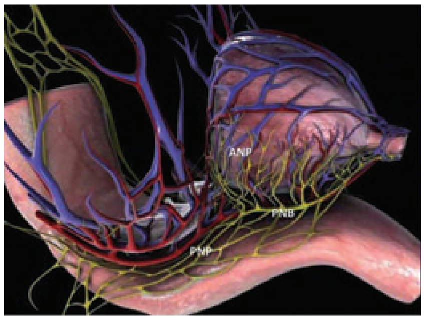


FIG. 12. *Neural hammock and trizonal neural architecture: PNP, ANP, and PNVB (PNB).*



hammock-like distribution of the nerves on which the prostate rests, showing that the NVB is more a network of multiple fine dispersed nerves than a distinct structure (Fig. 12) [16,17]. Kiyoshima *et al.* [18] also described that the dispersed nerve fibres are located between the prostate gland and the LPF. Furthermore, Eichelberg *et al.* [19] showed that only 46–66% of all nerves were found in the classical postero-lateral location relative to the prostate, while 21–29% were found on the antero-lateral surface.

Although the anatomical findings of the 1980s were important milestones for RP, those findings might not be applicable to state of the art RARP because the basic concept of pelvic neuroanatomy has been evolving as described above. Additionally, as the approach to the prostate in RARP is quite different from that in retropubic RP, i.e. an antegrade approach, we need to understand the anatomy around the proximal and posterior aspects of the prostate.

We proposed that the periprostatic nerves consistently fall into three broad surgically identifiable zones: the proximal neurovascular plate (PNP), the PNVB, and the accessory neural pathways (ANP) [12,20]. These nerves are arranged all around the prostate as a 'neural hammock', and thus we coined the term 'trizonal neural hammock' to describe the architecture of these nerves. The PNVBs are usually located in a postero-lateral groove on the side of the prostate. Significant variations in the location, shape, course, and composition of these bundles are present. They can be widespread on the rectum, Denonvilliers' fascia, and LPF, or circumscribed on the posterolateral groove enclosed in the triangular space. The PNVB is closely related to the prostatic pedicle and prostatic fascia, and its branches can sometimes be intermingled with the lateral pedicles of the prostate. Tissue planes may also be obliterated due to periprostatic inflammation, tumour-induced desmoplastic reaction, or EPE; resolving haemorrhage can make operative dissection difficult.

Correlating anatomical findings from cadaveric dissections with intraoperative video footage and final histology slides has led to the observation of accessory neural pathways in several locations around the prostate: between the prostatic and levator fascia, posterior to the prostate and in the layers of Denonvilliers' fascia, in several planes between the layers of periprostatic fascia, and even in the outermost edge of the prostate gland [7,8,21]. The superficial layer of Denonvilliers' fascia has cross-communicating fibres between the left and right NVBs. Distally, these bundles coalesce to form a retro-apical plexus [20]. In up to 35% of cases, this distal plexus penetrates the rectourethralis muscle. As this area is the final exit pathway for the cavernous and retro-apical nerves, these delicate structures may easily be damaged during urethral transection and anastomosis.

Menon *et al.* [22] recognised that numerous nerve bundles are present in the different layers of fascia enveloping the prostate. Deviating from Walsh's accepted technique of leaving the prostatic fascia on the RP specimen, Menon's group adopted an aggressive approach to NS termed the 'veil of Aphrodite' technique, wherein the prostatic fascia is dissected down to the glistening prostatic glandular surface, and the veil of periprostatic tissue is teased away in a relatively avascular plane [21,23]. Interposed between the prostatic fascia and the levator fascia are the periprostatic venous plexus and the neurovascular tissue that travel distally to supply the sphincter, urethra, and cavernosal tissue. These neural fibres travel close to the vessels;

occasionally, they can run independently, on the surface of the prostate, or laterally on the rectum. Some of these vessels remain just within the outer borders of the prostate ("subcapsular") for a short distance before dipping deeper into the prostatic tissue. Excessive blunt dissection of these vessels can create an artificial "transcapsular" plane resulting in an intraprostatic incision and a subsequent iatrogenic PSM.

In the present study, our results show that neural-hammock sparing during RARP was associated with improved potency outcomes; increased NS corresponded to increased percentages of patients who had intercourse and returned to baseline sexual function. Patients aged <60 years had better sexual function outcomes when compared with the whole group, but the same general trend between grade of NS and sexual function outcomes is preserved. The effort to balance oncological outcomes with functional outcomes through the risk-stratified approach can be evaluated through analysis of the PSM and EPE rates. PSM rates were not significantly higher with increased NS, while potency outcomes improved.

Furthermore, the increase in EPE rates from NS grade 1–4 supports the validity of the risk-stratified approach described in the present manuscript: the criteria for the risk-stratified approach were successful in identifying patients with lower risk of EPE for increased NS.

Our risk-stratified approach for determining the degree of NS based on the patient's likelihood of ipsilateral EPE seeks to categorize patients for optimal balance between oncological outcomes and functional outcomes. Our approach allows for more patients to have at least some form of NS, allowing for partial thickness/incremental NS that maintains low PSM rates while obtaining good sexual function outcomes. In all, 82% of the present patients underwent bilateral NS (NS grades 1 and 2), while 94% had at least some form of NS (NS grades 1–3). The overall PSM rate of the present patients was 9%. Patel *et al.* [24] reported 53% of patients undergoing bilateral, full NS with an overall PSM rate of 9.3%. Menon *et al.* [22] reported that 42% of patients underwent standard NS on both sides, 25% of patients had a unilateral 'veil of Aphrodite' with contralateral standard NS, and 33% of patients underwent a bilateral incremental NS; the overall PSM rate reported was 13%.

The present study is not without limitation. Our outcomes are based on one surgeon who has performed >3000 RARPs. The extensive experience of the surgeon may have influenced the potency outcomes of the present study, and thus, the outcomes results cannot be generalized. The study is also limited by the short follow-up periods, which can affect functional outcomes. A strength of the present study is that validated, self-administered SHIM questionnaires were used to evaluate potency rates. This is also one of the largest single institution and single surgeon studies investigating potency outcomes.

CONCLUSION

The risk-stratified approach and anatomical technique of neural-hammock sparing described in the present manuscript was effective in improving potency outcomes of patients without compromising cancer control. Patients with greater degrees of NS had higher rates of intercourse and return to baseline sexual function without an increase in PSM rates. Longer follow-up is necessary to elucidate the long-term effects of NS on oncological and sexual function outcomes. Further studies are also needed to determine the effects of NS on urinary continence.

CONFLICT OF INTEREST

Dr Ashutosh Tewari discloses that he is the principal investigator on research grants from Intuitive Surgical, Inc. (Sunnyvale, California, USA), the Prostate Cancer Foundation and the National Institute of Bioimaging and Bioengineering (R01 EB009388-01); he is also the endowed Ronald P. Lynch Professor of Urologic Oncology and Director of the LeFrak Institute of Robotic Surgery, Weill Cornell Medical College.

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Abbreviations: **(RA)RP**, (robot-assisted) radical prostatectomy; **HRQL**, health-related quality of life; **(P)NVB**, (predominant) neurovascular bundles; **NS**, nerve sparing; **SHIM**, sexual health inventory for men (questionnaire); **EPE**, extraprostatic extension; **eMRI**, endorectal MRI; **LPF**, lateral pelvic fascia; **PSM**, positive surgical margin; **IHP**, inferior hypogastric (pelvic) plexus; **PNP**, proximal neurovascular plate; **ANP**, accessory neural pathways.