Laparoscopy

Robotic Radical Prostatectomy with the “Veil of Aphrodite” Technique: Histologic Evidence of Enhanced Nerve Sparing

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Abstract

Objective: We have recently described a modification (Veil of Aphrodite) designed to preserve the lateral prostatic fascia (LPF) during robotic prostatectomy. Here, we histologically compare the Veil of Aphrodite technique (VT) and standard nerve-sparing technique (ST).

Methods: Thirty-six consecutive prostatectomies performed by a single surgeon were processed by the whole-mount method. The right and left anterolateral (AL) zones of each prostate were independently evaluated for LPF, plane of excision, capsular incision/margin status, margin clearance, and quantitative analysis of periprostatic nerve bundles using S100 immunostain.

Results: There were 42 AL zones with ST and 30 with VT. In all 42 ST zones, the plane of excision was outside the prostate and a rim of LPF was present. The mean margin clearance was 1.4 mm (0.6–2.8 mm) and the mean nerve bundle count was 10 (3–19). Capsular incision and margin status were negative in all 42. For VT, 24 of 30 zones lacked LPF and the plane of excision ran just by the prostatic edge. The mean margin clearance was 0.3 mm (0–1.7 mm) and the mean nerve bundle count was two (0–11). Two VT AL zones revealed capsular incision; the margin was negative for tumour in all 30. Differences in the margin clearances and nerve bundle counts between ST and VT were statistically significant (p < 0.0001).

Conclusions: The LPF contains nerve bundles that run along the surface of the AL zones. The VT is a safe procedure that effectively preserves the LPF and appears to provide enhanced nerve sparing as compared to the ST.

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1. Introduction

Despite relative improvements in potency rates with the advent of the “nerve-sparing” procedure, erectile dysfunction remains a major long-term morbidity for many men undergoing radical prostatectomy [1]. Even in skilled hands, the recovery of erectile function is variable and, in large reported series, potency rates following bilateral nerve sparing have ranged from 16% to 76% [2–4]. This lack of anticipated return of normal potency in a subset of men who undergo a “nerve-sparing” prostatectomy has been confounding. However, in recent years elucidation of key mechanisms involved in erection physiology has led to new insights regarding the topographic anatomy of erectile neural pathways [5]. Anatomic studies have demonstrated additional nerve fibers running on the lateral surface of the prostate, distinct from the classically described dorsolateral “neurovascular bundles,” with a significant role in neural stimulation to the cavernous tissue [5–7].

With the premise that under the magnification of the da Vinci robotic system preservation of lateral prostatic fascia (LPF) would be feasible and may result in improved postoperative potency, we have recently described a modification, the Veil of Aphrodite nerve-sparing technique (VT) [8]. Herein, we histologically analyse the prostatectomy specimens with conventional/standard nerve-sparing technique (ST) and VT to assess the anatomic attributes and feasibility of VT.

2. Methods

Thirty-six consecutive robotic prostatectomies (15, bilateral ST; 9, bilateral VT; 12, ST on one side and VT on the other) performed in a month by a single surgeon (M.M.) were included. These were performed after an experience of more than 1000 ST and 300 VT prostatectomies. The surgical techniques of these procedures, criteria for patient selection, and clinicopathologic data have been described previously [8–11]. A single urologic pathologist (A.S.), blinded to the nerve-sparing techniques, analysed the prostatectomy specimens.

The prostates were totally embedded and processed by a whole-mount method (Fig. 1). Each specimen was weighed, measured, and fixed in 10% neutral formalin. After painting the right half of the specimen with green ink and left half with black ink, a shave margin of the bladder neck was taken. The seminal vesicles and vas deferens were amputated near their junction with the prostate, sectioned, and entirely submitted. The prostate was then serially sectioned from apex to base at intervals of 4–5 mm, except the first (apex) and last (base) slices, which were kept 1.0 cm thick. The apex and base slices were then further sectioned in a radial fashion. All the intervening tissue slices were submitted as whole sections.

Because, from a technical standpoint, excision of each side of the prostatectomy is an independent event and a different nerve-sparing technique can be performed on either side, the two sides were individually analysed. As described previously [8], given that the primary difference between the two techniques is in the dissection of anterolateral (AL) zone, this was the focus of our analysis. These consisted of 1–4 o’clock (right) and 8–11 o’clock (left) zones (Fig. 1). Four-micron thick, hematoxylin and eosin-stained sections from the formalin-fixed paraffin-embedded tissue were examined microscopically and each AL zone was independently analysed for the following five parameters.

2.1. Periprostatic tissue (lateral prostatic fascia)

The presence or absence of periprostatic soft tissue was assessed. When present, its constituents, organization, and relationship with the prostate were noted.
2.2. **Plane of excision**

The tissue at the inked resection margin and the subjacent tissue forming the edge of each AL zone were evaluated to recognise the plane of excision.

2.3. **Capsular incision and margin status for tumour**

When a benign gland was seen in contact with the ink at the margin, it was considered capsular incision; the margin was positive when a malignant gland (tumour) was seen in contact with the ink. Both capsular incision and margin status were independently evaluated.

2.4. **Margin clearance**

For this study, we define margin clearance as the closest distance of either a benign gland or tumour from the inked margin. Using an ocular micrometer, margin clearance for each AL zone was recorded in millimeters. In the event of finding capsular incision or positive margin in an AL zone, its margin clearance was entered as zero.

2.5. **Nerve bundle count**

The presence and distribution of periprostatic neurovascular structures were histologically evaluated. A mid-gland whole-mount section of each prostate was immunostained with the S100 antibody (Dako, Carpinteria, CA, USA; 1:3000) for quantitative analysis of the nerves. Nerves and ganglia exclusively in the periprostatic location of AL zones were counted.

2.6. **Statistical analysis**

The differences in margin clearances and nerve bundle counts between the ST and the VT were evaluated using the paired t test and signed rank test of statistical significance, respectively. For each technique, the correlation between its margin clearance and nerve bundle count was also tested using the Pearson correlation. All statistical tests were two-sided and analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC).

3. **Results**

The 36 prostates came from men aged 45–75 yr (mean, 62 yr) and weighed from 22 to 148 g (mean, 51 g). A total of 72 AL zones were independently analysed. Forty-two of these were excised with ST and 30 with VT. The results are summarised in Table 1 and described below.

3.1. **ST**

In all 42 AL zones with ST, the plane of excision was well outside the limits of prostatic parenchyma and contained periprostatic soft tissue/LPF (Fig. 2). The borders of the prostate were recognised by the edges of compact fibromuscular prostatic stroma, which was either sharply demarcated or imperceptibly blended with the periprostatic tissue. This soft tissue or LBF was a multilayered structure, of variable thickness, comprising fibrous/collagenous bands, adipose tissue, vessels, and nerves (Fig. 3). In 22 AL zones, a condensed layer of fused fibrous bands (so-called capsule) encased portions of prostatic edge. Ventrally, the LBF became more condensed and merged with the anterior fibromuscular tissue. Three AL zones, with wider excisions, also contained portions of contiguous muscle. Capsular incision was absent and margins were negative for tumour in all 42. The closest distance of the margin from tumour was 0.7 mm. The mean margin clearance was 1.4 mm (range, 0.6–2.8 mm) and the mean periprostatic nerve bundle count was 10 (range, 3–19). These nerve bundles were distributed within the layers of LBF (Fig. 2C), travelling along the

<table>
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<th>Table 1 – Comparative analysis of two techniques</th>
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<tr>
<td><strong>Standard</strong></td>
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<tr>
<td>Number of anterolateral zones</td>
</tr>
<tr>
<td>Plane of excision</td>
</tr>
<tr>
<td>Lateral prostatic fascia</td>
</tr>
<tr>
<td>Capsular incision positive</td>
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<tr>
<td>Margin positive for tumour</td>
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<tr>
<td>Margin clearance (mm)</td>
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<td>Nerve bundle count</td>
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* Paired t test.
† Signed rank test.
surface of AL zones, and also seen in the fascial layers along the anterolateral portions of the apex. Of note, these periprostatic nerve bundles were generally larger than the minute subjacent intraprostatic nerve twigs. Also, periprostatic ganglions were identified in the LPF of eight of these zones.

3.2. VT

In 24 (80%) VT zones, the plane of excision ran just at the edge of the compact prostatic stroma (capsule), and no surrounding LPF was identified (Fig. 2D). In another five zones, the plane of excision was slightly outside the prostate with some periprostatic tissue (Fig. 4). The remaining AL zone no. 16 (Fig. 4) had a wider plane of excision and contained a decent rim of LPF. Overall, 2 (6.6%) AL zones revealed capsular incision; however, margin was negative for tumour in

Fig. 2 – Whole-mount section of prostate with standard technique (ST) on the left and Veil of Aphrodite technique (VT) on the right. (A) Entire whole-mount, hematoxylin and eosin (H&E). Note the tumour (red circle), presence of lateral prostatic fascia (LPF) on the left, and its absence on the right. For comparison, blue dotted line represents the plane of excision for VT, as has been done on the right. (B, H&E; C, S100; ×40). Matching area of left AL zone. Note the LPF with nerve bundles (blue arrows). Margin clearance (black arrow line) is 1.6 mm. (D, H&E; E, S100; ×40). Matching area of right AL zone. Note the absence of LPF and periprostatic nerve bundles. Margin clearance (black arrow line) is 0.3 mm.

Fig. 3 – LPF with fibrous bands (FB), nerve bundles (NB), and adipose tissue (AT). Blue arrow indicates the junction of LPF and prostatic stroma (PS). ×100.
all 30. The closest distance of the margin from tumour was 0.1 mm. The mean margin clearance was 0.3 mm (range, 0–1.7 mm) and in 27 (90%) zones, the margin clearance was ≤0.5 mm. The mean periprostatic nerve bundle count was two (range, 0–11).

3.3. Statistical analysis

The difference of margin clearances between the ST (1.46 ± 0.61 mm) and the VT (0.3 ± 0.32 mm) AL zones (Fig. 4) was statistically significant (p < 0.0001). Similarly, the difference in the number of nerve bundle counts (Fig. 5) between the ST (10 ± 3) and VT (2 ± 3) was statistically significant (p < 0.0001). For the VT (Fig. 6), the low number of nerve bundle counts was highly correlated with the small margin clearance (r = 0.87, p < 0.0001), whereas for ST (Fig. 7), the correlation of its margin clearance and nerve bundle count was not statistically significant (r = 0.25, p = 0.11).

4. Discussion

Erectile dysfunction is a potential sequela of radical prostatectomy. Due to its impact, in an era of rising number of younger men with prostate cancer detected by prostate-specific antigen (PSA), there is a pressing need for an effective intervention [12,13]. Initial anatomic description of “neurovascular bundles” by Walsh and Donker [14] formed the basis of developing a nerve-sparing operation to preserve erectile function after surgery. However, it was soon recognised that even a technically immaculate preservation of both “neurovascular bundles” does not guarantee a swift recovery to preoperative erectile status, and search for other avenues continued. In recent years, the traditional anatomic concept of “neurovascular bundles” has been challenged and our knowledge has been evolving [7,15,16]. It has been shown that some of the nerves innervating the cavernous
tissue are dispersed more laterally, within the LPF [5,17].

Since the inception of robotic laparoscopic prostatectomy, there has been an increasing interest in precise topographic anatomy of erectile nerves. Armed with the superior dexterity of movement, visualisation and sophistication of the robotic system, there is a unique prospect of accomplishing several surgical endeavours that were previously unfeasible. Undertaking one such modification, our VT designed to preserve the LPF, we have reported improved erectile outcomes [11,18]. However, it is not entirely clear whether the improved erectile outcomes are a result of enhanced nerve sparing, minimal traction injury due to antegrade dissection, or better preservation of vasculature [8].

Overall, we found distinct differences between the AL zones of ST and VT. First, LPF, containing neurovascular structures, was consistently recognised in the ST zones and was generally absent in the VT AL zones. As noted previously, by other investigators [19], we found that LPF is not a single fascial layer but a multilayered structure. In the study by Kiyoshima et al. [19], 52% cases contained significant adipose tissue in the LPF, whereas in the remaining 48%, fat was minimal and the layers of LPF were fused. This is in accordance with the variation we observed in the thickness of LPF and margin clearances of ST zones. Lunacek and coauthors [20] suggested that the quantity of neurovascular structures within this fascia can vary, partly due to variations in growth and volumes of prostate. This may explain the lack of correlation between the margin clearance and nerve bundle count of our ST zones (Fig. 7).

Ayala et al. [21] were first to advocate that prostate does not have a true capsule and we support this notion. Instead of a definite capsule, we observed that portions of prostatic stromal edge randomly merged with coalesced layer of periprostatic collagenous bands, which has been arbitrarily regarded as the “capsule.” The multilayered and loose arrangement of the LPF enables a plane to be developed at its interface with the compact prostatic parenchyma (Fig. 2). With the VT, we seek to get into this plane to dissect the LPF off the prostate [8]. Based on our results, it appears that this plane was found fairly consistently and LPF was preserved. In 27(90%) VT zones, margin clearance was ≤0.5 mm. The only outright exception was AL zone no. 16 (Figs. 4 and 5), in which all the parameters were similar to a ST zone and it seems LPF was not
preserved. In another two AL zones (no. 12 and no. 13), the plane of excision was a fraction wider than an ideal VT plane and these could be regarded as "semi-veils."

Another noteworthy finding in our study is the statistically significant difference between the nerve bundle counts of the two techniques (Fig. 5). Examining 79 non–nerve-sparing prostatectomy specimens, Kiyoshima et al. [19] demonstrated that 52% of prostates lacked a definite neurovascular bundle formation and vessels and nerves were spread throughout the lateral aspect. Consequently, it seems plausible that some of the nerve bundles we have recognised in the LPF innervate the cavernous tissue and perhaps some patients lose their potency after a prostatectomy due to severance of this accessory neural stimulus. It was beyond the scope of this study to determine the precise function of these nerves and it can be argued that these may be innervating the prostate or other adjacent structures. Nonetheless, mounting evidence indicates that nerve bundles in the LPF play a role in erectile function. Notably, we have recently reported improved postoperative potency rates following the VT. Of 154 consecutive patients who underwent the VT, 96% reported having intercourse at 1 yr and 71% recovered normal erectile function [11]. In a detailed fetal and adult anatomic study, Lunacek and colleagues [20] concluded that because of the growth and increasing volume of the prostate the cavernosal nerves are displaced laterally and anteriorly. Furthermore, Zvara et al. [5] verified that multiple nerve fibers on the lateral surfaces of the prostate were positive for nicotinamide adenine dinucleotide phosphate diaphorase, and transection of these nerves resulted in loss of electrically induced intracavernous pressure.

Because the distance of the tumour from the resection margin in a prostatectomy is generally very close, a foremost query with the preservation of LPF is the probability of iatrogenic positive margin. In a study of 278 margin-negative prostatectomy specimens by Emerson et al. [22], the mean closest distance between tumour and margin was 0.7 mm. Because preservation of LPF requires a plane of dissection much closer to the prostate,
there is a potential of violating its limits and causing positive margins. Mindful of this, only patients with low- and intermediate-risk cancers by the D’Amico classification are selected for the VT [8,11]. In this study, two (6.6%) VT AL zones revealed capsular incision and none of the margin was positive for tumour, but we stress that these results are based on exclusive evaluation of AL zones in a limited number of cases. Nonetheless, taking into account the margin results of our larger series [11], it appears that with VT, although there may be a slightly increased likelihood of capsular incision, the probability of tumour involving AL zone margin is low. One of the reasons seems to be the preferential posterior location of prostate cancer. In the study by Emerson et al. [22], the closest margin from the tumour was located in the posterior zones in 80% of the cases. Adhering to our criteria for patient selection, 7 of 135 (4.6%) VT patients with organ-confined disease had positive margins (six apical and one posterior), but none in the region of VT [11]. Therefore, for the VT, proper patient selection based on thorough clinical work-up and accurate needle biopsy interpretation is crucial.

5. Conclusions

We have demonstrated that the LPF, not preserved with the ST, does contain nerve bundles that run along the surface of the AL zones of prostate. The VT is a safe procedure that effectively preserves the LPF and appears to provide enhanced nerve sparing as compared to ST.

Conflict of interest: none

References

Editorial Comment
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The Authors present a complete and accurate pathological study to assess feasibility, oncological safety and qualitative/quantitative results of a modified nerve sparing robotic prostatectomy.

The issue to describe a technique that can guarantee both an anatomical approach with low oncological risks is certainly challenging but exciting.

The findings of this paper certainly help support evidence that robotic surgery can potentially detail the topographic and morphological landmarks of surgical anatomy particularly during radical prostatectomy, where accurate anatomical structure definition is essential.

These data confirm the growing evidence that neural tissue is present in the prostatic fascia covering the ventrolateral surface of the prostate and throughout the Denonvilliers’ fascia [1–3]. However their exact role in erectile function has yet to be completely defined.

The veil of Aphrodite technique (VT) with preservation of the prostatic fascia seems to significantly reduce the number of nerves present on the specimen, offering consistent quantitative data on a good nerve sparing technique. However, safety issues inevitably arise when considering the reduced margin clearance found on the VT specimens compared to standard nerve sparing (on average 0.3 mm compared to 0.7 mm). Further-
more, the low number of positive surgical margins described in both groups must be interpreted with caution and must be related to the limited number of cases performed and only partially to the techniques. The correlation between this enhanced nerve sparing technique and good clinical results remains still open due to many and diverse factors that can influence potency preservation. Although promising, the results may not be any better than standard nerve sparing prostatectomy, but expose the patient to higher risks of positive margins. Therefore, randomised clinical trials, with adequate patient selection and long term follow up using validated tools are required to assess the overall clinical impact of this robotic assisted technique on potency [4].

References


