Can Anterior Prostatic Fat Harbor Prostate Cancer Metastasis? A Prospective Cohort Study

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\section*{Key Words}
Anterior prostatic fat • Radical prostatectomy • Prostate cancer

\section*{Abstract}
\textbf{Objectives:} Traditionally anterior prostatic fat (APF) hasn’t been included in pelvic lymph node (LN) dissection templates following radical prostatectomy. In this study we evaluate the incidence of lymphoid tissue in the APF and the incidence of LN metastasis in APF in patients who have undergone robotic-assisted laparoscopic radical prostatectomy (RALP).

\textbf{Methods:} A prospective database of RALP has been maintained between January 2010 and September 2015. APF is routinely excised and sent separately for histopathological evaluation to identify lymphoid tissue and metastatic prostate cancer.

\textbf{Results:} A total of 629 underwent RALP. Forty-six (7.3\%) of the patients had lymphoid tissue on histopathological evaluation. Two patients had metastatic disease. Both patients with positive LNs were intermediate risk on pre-operative evolution (A-PSA 16.6 ng/ml, Gleason 3 + 4; B PSA 7.3 ng/ml, Gleason 4 + 3) and upgraded on final prostate pathological evaluation to high risk disease (A-Gleason 4 + 5, pT3b, B-Gleason 4 + 3, pT4).

\textbf{Conclusion:} There appears to be lymphatic drainage to the APF from the prostate. Hence APF should be included in pelvic LN dissection templates when lymphadenectomy is contemplated in patients undergoing radical prostatectomy.
Overall, 629 consecutive patients who underwent RALP between January 2010 and September 2015 were included in our study. Surgical procedures were performed by 3 robotic surgeons (J.A., T.L. and N.V.). All of the RALP procedures were performed via a transperitoneal approach.

During the RALP procedures, APF tissue samples were sent separately for pathologic evaluation. APF covering prostate, dorsal venous complex, prostatic apex, puboprostatic ligaments, prostate-vesical junction and the bladder neck was dissected en bloc laterally and cephalad.

Parameters including serum prostate specific antigen (PSA), prostate weight and Gleason score were included for further evaluation.

### Results

Patient characteristics are summarized in Table 1. Mean patient age and serum PSA were 62.2 ± 5.8 years (range 39–76 years) and 8.9 ± 6.2 ng/ml (range 1–42 ng/ml), respectively. Overall, LNs in APF tissues were detected in 45 (7.1%) patients with a mean LN yield of 1.1 ± 0.7 LNs (range 1–3). Among those found, only 2 patients had positive LN (0.3%).

Patients with LNs in their APF 4 of them in pT3a disease, 7 in pT2c, 2 in pT2b, 22 in pT2a, 9 in pT1c and 1 in pT1a. Patients with positive LNs were pT2c and pT3a, and upgraded on final prostate histopathology to pT3b and pT4. Patients with LNs had Gleason score of 3 + 3 = 6 in 16 patients, 3 + 4 = 7 in 21 patients, 4 + 3 = 7 in 7 patients and only one had Gleason score of 4 + 4 = 8. The 2 patients with LNs had Gleason 3 + 4 and 4 + 3 and upgraded on final prostate pathological evaluation to Gleason 4 + 3 and 4 + 5, respectively.

### Discussion

In our study, we identified LNs in APF tissue in 7.1% (n = 629) of the patients. Aning et al. [6] reported 17% (n = 282), Jeong et al. [7] reported 11.6% (n = 228), Finley et al. [8] reported 14.7% (n = 204) and Atmaca et al. [11] reported 10% (n = 129) LNs in APF tissue in their series, respectively. Therefore, our findings are less than all the previously published studies. Our study has longer series of patients 629 done over 5 years.

In our study, metastatic LN was detected in 2 (0.3%) out of 629 patients that was obtained from the APF tissue region overlying the prostate. However, Finley et al. [8] found LN metastasis in 4 of 204 patients and Jeong et al. [7] found LN metastasis in 3 of 228 patients in their series. In the published literature, LN metastasis rate in anterior periprostatic lymphoid tissue varied between 1.2 and 2.5% [7–10]. In our study, it was only 0.3%. In a multi-center study, Kim et al. [10] included 4,261 RRP and RALP patients and there were 40 patients who had metastasis on periprostatic LNs.

The outcomes of published literature on APF tissue and presence of LNs are listed in Table 2.

The European Association of Urology [12] and National Comprehensive Cancer Network [13] recommend extended pelvic LN dissection in patients at 10% or greater and 7% or greater calculated risk, respectively, for LN metastases. The American Urological Association recommends pelvic LN dissection in patients at higher risk for nodal involvement [14]. Prognostic significance of LN metastases in PCa [15] and assessment of rates of LNs and LN metastases in periprostatic fat pads in radical prostatectomy were reported before [16]. We removed APF tissue in all our patients (low, intermediate and high-risk) and sent it separately for histopathologic evaluation in order to identify the presence of LNs and possible metastasis to identify the correct stage of the disease.

Kim et al. [10] suggested that removal of APF tissue leads to more accurate staging of the patients. In their series, due to the identification of metastatic LNs in the APF tissue, 0.63% of the patients were up-staged pathologically [10]. This finding might certainly have an impact on postoperative adjuvant treatment requirement in this patient group.

Involvement of the regional LNs is a very important prognostic indicator of disease-free survival and overall survival in PCa [15]. Metastatic LN is detection in APF tissue might necessitate adjuvant hormone therapy or radiotherapy. In our study, the 2 patients (0.3%) who had the metastatic nodes only one of them needed post operative adjuvant radiotherapy. To assess the need of adjuvant therapy, postoperative serum PSA follow-up is important as well as detecting metastatic LNs.
We always perform APF tissue as en bloc excision, while Kim et al. [10] separately evaluated APF tissue in 3 pieces as a left packet, middle packet and a right packet. In their results, 89% of the LNs were detected in the middle packet [10]. They suggested separately dissecting and sending APF tissue for pathologic evaluation.

Not only robotic prostatectomies have evaluated LN existence in APF tissue but also it was assessed in open RRP series. Hansen et al. [16] identified LNs in periprostatic region in 19 (5.5%) patients of 356 in their RRP series and 4 (1.2%) of them had metastasis. In this study they reported that there is no connection between periprostatic LN metastasis and pelvic LN metastasis, but in order to provide exact staging, pathologic examination of periprostatic lymphatic area should be a routine procedure.

Table 2. The outcomes of published literature on APF tissue and presence of LNs

| Reference            | Year | Robotic or open | Patient number | Presence of LNs (n, %) | Presence of LN metastasis (n, %) |
|----------------------|------|----------------|----------------|------------------------|---------------------------------|
| Kim et al. [10]      | 2013 | both           | 4,261          | 388, 11.9%             | 40, 0.94%                       |
| Finley et al. [8]    | 2007 | robotic        | 204            | 30, 14.7%              | 4, 2%                           |
| Jeong et al. [7]     | 2013 | robotic        | 258            | 30, 11%                | 3, 1.16%                        |
| Atmaca et al. [11]   | 2015 | robotic        | 129            | 14, 10.9%              | 0, 0%                           |

Our study we had a fair number of patients only small number of patients (0.3%) showed metastatic nodes in the APF tissue. With increasing number of patients and having more high-risk PCA patients, we think more patients with metastatic LNs in the APF tissue might be identified.

**Conclusion**

There appears to be lymphatic drainage to the anterior prostatic fat from the prostate. Hence APF should be included in pelvic LN dissection templates when lymphadenectomy is contemplated in patients undergoing radical prostatectomy.

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