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

Mohannad Hosny^a Bhavan Rai^a Feras Aljaafari^a Samita Agarwal^b
Thomas McNicholas^a Gregory Boustead^a Timothy Lane^a
James Adshead^a Nikhil Vasdev^a

^aHertfordshire and South Bedfordshire Urological Cancer Centre, Department of Urology; ^bDepartment of Histopathology, Lister Hospital, Stevenage, UK

Key Words

Anterior prostatic fat • Radical prostatectomy • Prostate cancer

Abstract

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 robot-assisted laparoscopic radical prostatectomy (RALP). **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. **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). **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.

Copyright © 2016 S. Karger AG, Basel

Introduction

Radical prostatectomy involves removal of the entire prostate gland between the urethra and bladder, and resection of both seminal vesicles, along with sufficient surrounding tissue to obtain negative margins. Often, this procedure is accompanied by bilateral pelvic lymph node (LN) dissection [1].

Robot-assisted laparoscopic prostatectomy (RALP) is displacing radical retropubic prostatectomy (RRP) as the most used surgical approach for clinically localized prostate cancer (PCa) in the USA and is being increasingly used in Europe and other parts of the world [2].

The number of involved nodes [3], the tumor volume within the LN, and capsular perforation of the nodal metastases are predictors of early recurrence after prostatectomy for nodal metastasized PCa [4].

The fatty tissue overlying the prostate is usually removed in order to have a better exposure of the dorsal venous complex, the puboprostatic ligaments, and the prostate apex [5]. This fatty tissue is examined separately by the pathologist for the presence of LNs and possible metastasis. If this fatty tissue is missed, it might have an impact on the postoperative disease stage, treatment, and oncologic outcomes.

In our study, we evaluated the anterior prostatic fat (APF) tissues that were separately sent for histopathology in order to examine presence of LNs and metastasis.

Table 1. Patient characteristics

Patients	Patients with LN(s) in APF	Patients with positive LN(s) in APF	Total
Age, years	63.5 ± 6.5	59.5 ± 8.5	62.2 ± 5.8
PSA, ng/ml	11.6 ± 1.5	11.95 ± 4.6	8.9 ± 6.2

Materials and Methods

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, puboprostic 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.

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%

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.

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.

References

- 1 Bianco FJ Jr, Scardino PT, Eastham JA: Radical prostatectomy: long-term cancer control and recovery of sexual and urinary function ("trifecta"). *Urology* 2005;66(5 Suppl):83–94.
- 2 Gandaglia G, Sammon JD, Chang SL, Choueiri TK, Hu JC, Karakiewicz PI, Kibel AS, Kim SP, Konijeti R, Montorsi F, Nguyen PL, Sukumar S, Menon M, Sun M, Trinh QD: Comparative effectiveness of robot-assisted and open radical prostatectomy in the post-dissemination era. *J Clin Oncol* 2014;32:1419–1426.
- 3 Burkhard FC, Schumacher M, Studer UE: The role of lymphadenectomy in prostate cancer. *Nat Clin Pract Urol* 2005;2:336–342.
- 4 Ploussard G, Briganti A, de la Taille A, Haese A, Heidenreich A, Menon M, Sulser T, Tewari AK, Eastham JA: Pelvic lymph node dissection during robot-assisted radical prostatectomy: efficacy, limitations, and complications—a systematic review of the literature. *Eur Urol* 2014;65:7–16.
- 5 Ahlering TE, Eichel L, Edwards RA, Lee DI, Skarecky DW: Robotic radical prostatectomy: a technique to reduce pT2 positive margins. *Urology* 2004;64:1224–1228.
- 6 Aning JJ, Thuraiaraja R, Gillatt DA, Koup-paris AJ, Rowe EW, Oxley J: Pathological analysis of lymph nodes in anterior prostatic fat excised at robot-assisted radical prostatectomy. *J Clin Pathol* 2014;67:787–791.
- 7 Jeong J, Choi EY, Kang DI, Ercolani M, Lee DH, Kim WJ, Kim IY: Pathologic implications of prostatic anterior fat pad. *Urol Oncol* 2013;31:63–67.
- 8 Finley DS, Deane L, Rodriguez E, Vallone J, Deshmukh S, Skarecky D, Carpenter P, Narula N, Ornstein DK, Ahlering TE: Anatomic excision of anterior prostatic fat at radical prostatectomy: implications for pathologic upstaging. *Urology* 2007;70:1000–1003.
- 9 Yuh B, Wu H, Ruel N, Wilson T: Analysis of regional lymph nodes in periprostatic fat following robotassisted radical prostatectomy. *BJU Int* 2012;109:603–607.

- 10 Kim IY, Modi PK, Sadimin E, Ha YS, Kim JH, Skarecky D, Cha DY, Wambi CO, Ou YC, Yuh B, Park S, Llukani E, Albala DM, Wilson T, Ahlering T, Badani K, Ahn H, Lee DI, May M, Kim WJ, Lee DH: Detailed analysis of patients with metastasis to the prostatic anterior fat pad lymph nodes: a multi-institutional study. *J Urol* 2013;190:527–534.
- 11 Atmaca AF, Canda AE, Keske M, Arslan ME, Kamaci D, Alkan E, Balbay MD: Does anterior prostatic fat tissue removed during robotic radical prostatectomy contain any lymph nodes? *Cent European J Urol* 2015; 68:410–414.
- 12 Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, Mason M, Matveev V, Wiegel T, Zattoni F, Mottet N: EAU guidelines on prostate cancer. *European Association of Urology*; 2014.
- 13 National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology 2012. Prostate Cancer.
- 14 Thompson I, Thrasher JB, Aus G, Burnett AL, Canby-Hagino ED, Cookson MS, D'Amico AV, Dmochowski RR, Eton DT, Forman JD, Goldenberg SL, Hernandez J, Higano CS, Kraus SR, Moul JW, Tangen CM: Guideline for the management of clinically localized prostate cancer: 2007 update. *J Urol* 2007;177:2106–2131.
- 15 Gervasi LA, Mata J, Easley JD, Wilbanks JH, Seale-Hawkins C, Carlton CE, Jr, Scardino PT: Prognostic significance of lymph nodal metastases in prostate cancer. *J Urol* 1989; 142:332–336.
- 16 Hansen J, Budäus L, Spethmann J, Schlomm T, Salomon G, Rink M, Haese A, Steuber T, Heinzer H, Huland H, Graefen M, Michl U: Assessment of rates of lymph nodes and lymph node metastases in periprostatic fat pads in a consecutive cohort treated with retropubic radical prostatectomy. *Urology* 2012;80:877–882.