

Research Paper

Impact of prostatic anterior fat pads with lymph node staging in prostate cancer

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Abstract

Background: Several reports have revealed the presence of lymph nodes in the prostatic anterior fat pad (PAFP). To date, no study has described the characteristics of Taiwanese patients harboring PAFP lymph nodes with metastatic prostate cancer involvement.

Method: Between December 2006 and May 2015, a total of 849 consecutive patients underwent robot-assisted laparoscopic radical prostatectomy with PAFP dissection. Pathological examination of the dissected PAFP was conducted to assess the presence of lymphoid tissue and prostate cancer involvement.

Results: Of the 849 patients, 76 (9.0%) had 1–3 PAFP lymph nodes. Moreover, 11 (1.3%) of the 76 patients had positive lymph node metastases of prostate cancer in the PAFP; 5 (0.6%) of the 11 patients, who had negative pelvic lymph node involvement, were upstaged because of positive metastases in PAFP lymph nodes. Among the 76 patients having PAFP lymph nodes, metastatic lymph nodes were associated with the clinical T stage, preoperative Gleason score, pathological T stage, and pathological N stage ($p < 0.001$). Patients with pathological seminal vesicle invasion and a higher surgical Gleason score also exhibited PAFP lymph node metastases ($p < 0.005$).

Conclusion: Our data show that 9.0% of patients had PAFP lymph nodes and that 1.3% had prostate cancer metastases. Additionally, 0.6% of patients were upstaged because of positive metastases in PAFP lymph nodes. Because of the pathological analysis of the PAFP, a few patients were upstaged. Thus, routine pathological analysis of the PAFP should only be conducted for those with higher preoperative prostate-specific antigen, higher Gleason score, and advanced T stage observations.

Key words: Lymph nodes, prostatic anterior fat pad, prostate cancer

Introduction

Pelvic lymph node dissection (PLND) is the most common method for nodal staging in prostate cancer patients undergoing radical prostatectomy (RP) [1-3]. PLND provides valuable information about the starting time of adjuvant radiotherapy and androgen deprivation therapy and may have a therapeutic

benefit in prostate cancer patients [3, 4]. Some series have shown high cancer-specific survival rates for patients with only one or two lymph node metastases after extended lymphadenectomy [5, 6].

The prostatic anterior fat pad (PAFP) refers to the adipose tissue anterior to the prostate. PAFP

excision is recommended in patients treated with RP to aid in the identification of the prostatic apex, dorsal venous complex, and bladder neck [7, 8]. Several series have reported the presence of PAFP lymph nodes, some of which had metastatic prostate cancer involvement, resulting in disease upstaging in patients with negative pelvic node involvement [8-16]. Manny et al. [17] injected indocyanine green (ICG) into the prostate before RP and could detect lymphatic drainage in the PAFP. In our hospital, since 2006, the PAFP has been routinely removed during robot-assisted laparoscopic radical prostatectomy (RALRP) for more effective anatomical identification, with the dissected PAFP being sent for separate pathological analysis. Based on these data, in this study, we analyzed the rate of the presence of PAFP lymph nodes and the risk factors for PAFP lymph nodes metastases.

Materials and Methods

Patients

This study was approved by the Institutional Review Boards of Taichung Veterans General Hospital (TCVGH) and Tungs' Taichung MetroHarbor Hospital (TTMHH). Moreover, this study was exempted from obtaining informed consent because of its retrospective design. In this study, only men with prostate cancer who underwent RALRP with PAFP excision and PLND during the same operation from December 2006 to May 2015 were included. Patients undergoing conventional prostate surgery and laparoscopic prostate surgery were excluded. A total of 849 consecutive prostate cancer patients undergoing RALRP performed by a single surgeon at the two hospitals met the criteria. The preoperative diagnosis of prostate cancer was based on transrectal prostate biopsy or transurethral prostate resection. Patients were initially diagnosed at TCVGH or TTMHH or were referrals from other hospitals. The pathological grading of the transrectal prostate biopsy sample was conducted using the Gleason grading system. Cancer with clinical T stages from T1 to T3 was categorized as localized prostate cancer. The presence of nodal or bony metastasis was detected by preoperative image surveys such as computed tomography, magnetic resonance imaging, or technetium-99m bone scan. Preoperative work-up included measuring the prostate-specific antigen (PSA) level and assessing the clinical stage assigned by attending urologists. The pretreatment PSA level was measured before digital rectal examination and transrectal ultrasound. Moreover, PAFP dissection was performed in a caudal-cranial direction to the bladder neck. The boundaries of PAFP dissection

were caudate to the prostate apex, superiorly to the pubic arch, inferiorly to the prostate, laterally to the edges of the prostate joining the endopelvic fascia, and cephalad to the bladder neck. All patients underwent PAFP excision before prostatectomy and bilateral PLND. For pathological analysis, PAFP, right PLND, and left PLND were placed in three separate containers.

Statistical Analysis

Data analysis was performed using the statistical analysis system (SAS). A two-sided Student's *t* test was used to determine the differences in continuous data, and a chi-squared test or Fisher exact test were used to compare differences in categorical data.

Results

The PAFP tissue of 849 patients was analyzed pathologically. Of the 849 patients, 76 (9.0%) had 1 to 3 lymph nodes in their PAFP. Moreover, 63 patients had only 1 lymph node, 10 patients had 2 lymph nodes, and 3 patients had 3 lymph nodes, with an average of 1.2 nodes per patient. Metastatic prostate cancer was detected in PAFP lymph nodes in 11 patients (1.3%).

The preoperative characteristics of patients with and without lymph nodes in the PAFP are shown in Table 1. Patients with PAFP lymph nodes tended to have a higher clinical T stage ($p < 0.05$). No differences were observed in patients' age, body mass index, prostate weight, PSA, or preoperative Gleason score.

Table 1. Demographics comparing patients with lymph nodes present or absent in prostatic anterior fat pad (PAFP).

Variable	Lymph nodes absent in PAFP (n=773)	Lymph nodes present in PAFP (n=76)	p value
Age at surgery, Mean \pm SD	65.71 \pm 7.73	66.76 \pm 7.88	0.256
BMI, Mean \pm SD	24.76 \pm 3.03	24.98 \pm 3.14	0.549
Prostate weight, Mean \pm SD	41.57 \pm 19.25	45.54 \pm 21.82	0.103
PSA, n (%)			
0-10	339 (43.9%)	36 (47.4%)	0.069
10-20	255 (33.0%)	16 (21.1%)	
>20	179 (23.1%)	24 (31.6%)	
Preoperative Gleason Score, n (%)			
2-6	375 (48.5%)	34 (44.7%)	0.093
7	253 (32.7%)	20 (26.3%)	
8-10	145 (18.8%)	22 (29.0%)	
Clinical T stage, n (%)			
T1abc	239 (30.9%)	19 (25.0%)	0.002
T2/T2a/T2b	249 (32.2%)	17 (22.4%)	
T2c	214 (27.7%)	23 (30.3%)	
T3	71 (9.2%)	17 (22.4%)	

Table 2 lists the surgical and pathological data of the two groups. The presence of PAFP lymph nodes was related to more aggressive prostate cancer with seminal vesicle invasion and a higher Gleason score.

Moreover, metastatic prostate cancer in pelvic lymph nodes showed a strong association with the presence of PAFP lymph nodes ($p < 0.001$).

Table 2. Surgical and pathologic data comparing patients with lymph nodes present or absent in prostatic anterior fat pad (PAFP).

Variable	Lymph nodes absent in PAFP (n=773)	Lymph nodes present in PAFP (n=76)	p value
Pathological T stage, n (%)			
pT2	315 (40.8%)	32 (40.8%)	0.518
pT3	428 (55.4%)	39 (52.6%)	
pT4	30 (3.8%)	5 (6.6%)	
Seminal vesicle invasion, n (%) #			
Negative	610 (82.1%)	48 (67.6%)	0.003
Positive	133 (17.9%)	23 (32.4%)	
pN stage, n (%)			
pN-	721 (93.3%)	62 (81.6%)	<0.001
pN+	52 (6.7%)	14 (18.4%)	
Surgical Gleason Score, n (%)			
≤6	195 (25.2%)	17 (22.4%)	0.030
7	432 (55.9%)	35 (46.1%)	
8-10	146 (18.9%)	24 (31.3%)	

Seminal vesicle invasion: pT2 and pT3 cases.

Of the 76 patients with PAFP lymph nodes, 11 (1.3%) had positive prostate cancer metastases. Table 3 presents an analysis of the characteristics of patients having positive PAFP lymph node metastases and those having negative PAFP lymph node metastases. Higher preoperative PSA, Gleason score, and clinical T stage observations were correlated with the presence of lymph node metastases of prostate cancer.

Table 3. Demographics comparing patients with lymph nodes metastasis present or absent in prostatic anterior fat pad (PAFP).

Variable	Lymph nodes metastasis absent in PAFP (n=65)	Lymph nodes metastasis present in PAFP (n=11)	p value
Age at surgery, Mean ± SD	66.40 ± 7.38	68.91 ± 10.53	0.332
BMI, Mean ± SD	24.95 ± 3.23	25.19 ± 2.70	0.815
Prostate weight, Mean ± SD	45.62 ± 23.04	44.18 ± 13.07	0.841
PSA, n (%)			
0-10	34 (52.3%)	2 (18.2%)	0.006
10-20	15 (23.1%)	1 (9.1%)	
>20	16 (24.6%)	8 (72.7%)	
Preoperative Gleason Score, n (%)			
2-6	34 (52.3%)	0 (0%)	<0.001
7	19 (29.2%)	1 (9.1%)	
8-10	12 (18.5%)	10 (90.9%)	
Clinical T stage, n (%)			
T1abc	19 (29.2%)	0 (0%)	<0.001
T2/T2a/T2b	15 (23.2%)	2 (18.2%)	
T2c	22 (33.8%)	1 (9.1%)	
T3	9 (13.8%)	8 (72.7%)	

Table 4 shows a comparison of the postoperative parameters of patients with and without metastases in PAFP lymph node. Statistically significant differences

were observed in patients' pathological T stage ($p < 0.001$), seminal vesicle invasion, concomitant pelvic lymph node metastases ($p < 0.001$), and surgical Gleason score between the two groups.

Table 4. Surgical and pathologic data comparing patients with lymph nodes metastasis present or absent in prostatic anterior fat pad (PAFP).

Variable	Lymph nodes metastasis absent in PAFP (n=65)	Lymph nodes metastasis present in PAFP (n=11)	p value
Pathological T stage, n (%)			
pT2	31 (47.7%)	0 (0%)	<0.001
pT3	33 (50.8%)	7 (63.6%)	
pT4	1 (1.5%)	4 (36.4%)	
Seminal vesicle invasion, n (%)#			
Negative	46 (71.9%)	2 (28.6%)	0.020
Positive	18 (28.1%)	5 (71.4%)	
pN stage, n (%)			
pN-	62 (95.4%)	0 (0%)	<0.001
pN+	3 (4.6%)	11 (100%)	
Surgical Gleason Score, n (%)			
≤6	17 (26.2%)	0 (0%)	0.005
7	32 (49.2%)	3 (27.3%)	
8-10	16 (24.6%)	8 (72.7%)	

Seminal vesicle invasion: pT2 and pT3 cases.

Five patients (0.6%) were upstaged because of the derivation of positive results for metastatic prostate cancer in PAFP lymph nodes but negative findings for PLND. The clinicopathological characteristics of these patients are shown in Table 5. prostate cancer stages classified as stages IIb and III according to the American Joint Committee on Cancer were upstaged to stage IV after positive metastases in PAFP lymph nodes were found. Patients upstaged to stage IV had high risks preoperatively according to D'Amico classification.

Table 5. The characteristics of the 5 upstaging patients.

Patient	Age	Pre-op PSA	Pre-op Gleason score	cT stage	Surgical Gleason score	pT stage	PAFP lymph node pos./total	Pelvic lymph node Pos. /total
1	71	11.7	4+5	T2b	4+5	T3b	1/1	0/6
2	45	26.0	5+3	T3a	5+3	T3b	1/1	0/9
3	62	112	5+4	T3a	4+3	T3b	1/1	0/13
4	74	25.5	4+5	T3a	5+4	T3b	1/1	0/10
5	65	7.1	4+3	T2c	3+4	T3a	1/1	0/13

Discussion

To the best of our knowledge, this is the first report showing the prevalence of PAFP lymph nodes with or without prostate cancer involvement among Taiwanese patients. To avoid surgical technique differences, we collected the data of consecutive patients undergoing RALRP performed by a single surgeon who had the largest patient volume. Our data demonstrate that of a total of 849 patients who

underwent RALRP, 9.0% harbored PAFP lymph nodes, 1.3% had metastatic prostate cancer, and 0.6% were upstaged because the pathological analysis of the PAFP revealed positive metastases in PAFP lymph nodes.

Dissection of the PAFP provides a clearer view of the prostate apex, puboprostatic ligament, dorsal venous complex, and bladder neck. Ahlering et al. [7] initially reported a technique for reducing positive surgical margins during RALRP. They found that dissecting the PAFP off the anterior surface of the prostate and dorsal venous complex could delineate the entire apex of the prostate. This could considerably reduce the positive apical surgical margin rate [7]. They also demonstrated that the PAFP contains lymph nodes and may be upstaged because of positive prostate cancer metastases [8]. Recently, several studies have demonstrated 9%–17% of PAFPs to contain lymph nodes (Table 6) [8-16, 18].

Table 6. Summary of prostatic anterior fat pad (PAFP) studies.

Study	N	Open RRP, n	Lymph nodes present in PAFP, n (%)	Lymph nodes metastasis present in PAFP lymph nodes, n (%)	Upstage, n (%)
Finley et al. [8]	204	0	30 (14.7)	4 (2)	3 (1.47)
Yuh et al. [10]	120	0	20 (16.7)	3 (2.5)	3 (2.5)
Hansen et al. [18]	356	356	19 (5.5)	4 (1.2)	0
Jeong et al. [9]	258	0	30 (11.6)	3 (1.2)	1 (0.39)
Kim et al. [11]	4,261	124	388 (11.9)	40 (0.94)	27 (0.63)
Aning et al. [12]	282	0	49 (17)	4 (1.4)	3 (1.06)
Ozkan et al. [13]	100	0	9 (9)	0	0
Atmaca et al. [14]	129	0	14 (10.9)	0	0
Ball et al. [15]	2,413	1,266	255 (10.6)	14 (0.6)	0
Kwon et al. [16]	8,800	N/A	206 (2.3)	88 (0.1)	63 (0.07)
Present study	849	0	76 (9)	11 (1.3)	5 (0.6)

For patients undergoing RP as the definitive treatment, accurate staging is important to identify patients at risk of disease progression. Previous studies have described that lymphatic drainage of the prostate can be performed through the external iliac, obturator, hypogastric, and presacral lymph nodes [19, 20]. Manny et al. [17] injected ICG into the prostate before RP and reported that 13% of patients had detectable fluorescence in the PAFP. They concluded that ICG is highly sensitive but relatively nonspecific for the detection of nodal metastasis. These observations suggest that performing pathological analysis of the PAFP leads to more accurate staging. In our series, PAFP lymph nodes were found in few patients; however, 14.5% (11 of 76) of the patients harbored malignancy in PAFP lymph nodes compared with 6.8% (58 of 849) of the patients harboring metastases in pelvic lymph nodes. In published series, the rate of metastatic prostate cancer in PAFP lymph nodes ranges from 0.6% to 2.5% (Table 6) [8-16, 18]. Two studies have included patients undergoing open radical retropubic

prostatectomy (RRP). We determined that the percentage of patients with metastatic PAFP lymph nodes was higher in the RALRP series than in the open RRP series. It is possible that open surgery does not provide as much PAFP tissue as robotic surgery does.

In addition to increasing staging accuracy, the removal of micrometastatic nodes increases the biochemical recurrence (BCR)-free rate [21, 22] and the cancer-specific survival rate in patients treated with PLND [23]. Increased nodal removal during PLND results in more accurate staging and an improved survival rate [24, 25]. Moreover, Altok et al. has shown that prostate cancer was also upstaged during robot-assisted radical prostatectomy (RARP) [26]. In our study, five patients who were upstaged had intermediate or high risks preoperatively according to D'Amico classification. This finding is consistent with those of other series [9, 10]. Moreover, as shown in table 5, no cases with Gleason score 6 had metastatic disease to PAFP. Thus, the beneficial effects in patients with Gleason score 3+3 need to be further investigated.

Our study demonstrated that only the preoperative T stage was associated with the presence of PAFP lymph node. However, comparison of patients with metastatic PAFP lymph nodes and those without metastatic PAFP lymph node revealed that higher preoperative PSA, Gleason score, and T stage observations were strongly associated with the presence of lymph node metastases of prostate cancer.

Despite having the strength of consecutive cases and the largest sample size to date among studies of Taiwanese patients, our study is not without limitations. First, we could not conduct long-term follow-up to evaluate the effect of PAFP lymph node removal on BCR rates. Second, because only a few patients were upstaged, we could not compare the categorical data of the two groups: PAFP lymph node (+)/pelvic lymph node (-) and PAFP lymph node (-)/pelvic lymph node (+). Finally, because all patients underwent PAFP removal, we could not determine whether PAFP removal benefits patients. Therefore, additional prospective and categorical analyses with longer follow-up are warranted.

In conclusion, PAFP excision before RP was associated with limited surgical complications and no related morbidity. PAFP excision facilitates achieving a clearer view of the prostate anatomic structure and surgical landmarks. Therefore, we recommend that the PAFP should be removed in all patients during RP, but the routine pathological analysis of the PAFP should only be conducted for those with a high-risk prostate cancer.

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Competing Interests

The authors have declared that no competing interest exists.

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