ORIGINAL ARTICLE

Gulhane Med J 2018;60: 19-25

doi: 10.26657/gulhane.00011

Pathology results, complications of prostate biopsies and correlation with radical prostatectomy: Analysis of 1509 patients

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ABSTRACT

Aims: Prostate cancer is a global health problem and the second most common cancer in men. In this study, we aimed to analyse the pathologic results, complications of prostate biopsies and the comparison of histopathologic results with the results of radical prostatectomy.

Methods: 1509 patients who underwent TRUS-guided prostate biopsy in Kecioren Training and Research Hospital between January 2008 and January 2017 were included in the study.

Results: 1116 patients were diagnosed as BPH and 393 patients were as PCa. Average PSA level was 9,27ng/ml for BPH group. 52 patients had urinary tract infections after prostate biopsy for BPH group and one had severe hemorrhage. The average age of PCa group was 67,3 years. Average PSA level was 29,87ng/ml.

Conclusions: Despite the importance of TRUS-guided prostate biopsy in diagnosis of PCa, the present study showed inaccuracy when compared to the result of the radical prostatectomy.

Key words: *prostate, biopsy, pathology, complication, prostate, cancer*

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Date submitted: Fab 11, 2018 • **Date accepted:** Mar 06, 2018 • **Online publication date:** March 15, 2018

Introduction

Prostate cancer is a global health problem and the second most common cancer in men.(1) The incidence is variable for different countries and regions.(1-3) It is nearly 35 to 37.6 in 100000 men for Turkey.(2) The incidence of prostate cancer increased with the increased life expectancy and the change of dietary habits.(4) Prostate specific antigene(PSA), digital rectal examination(DRE), transrectal ultrasonography(TRUS) and magnetic resonance imaging(MRI) is widely used for the diagnosis of prostate cancer.(4) PSA is one of the basic serum biomarkers for prostate cancer.(1) DRE has low sensitivity itself because there are other variables related with it such as inflammation benign prostatic hyperplasia and age.(5) Transrectal ultrasonography(TRUS) and TRUS-guided prostate biopsy remains the gold standart for prostate cancer diagnosis.(5) Elevated PSA level and/or abnormal digital rectal examination finding are the main indications for TRUS-guided prostate biopsy. Different PSA cutoff levels are used for biopsy decision.(2) Also different nomograms are used for populations.(6) Partin et al. developed and reported nomograms that can be used for the prediction of nodal metastasis and pathologic stage.(7) In our clinic we use the age age-specific ranges of PSA. Several studies have been conducted to reveal the accuracy of prostate biopsy as comparing it with radical prostatectomy pathology results. Bulbul et al. reported low prediction of prostate biopsy.(8) Besides the diagnostic level of TRUS-guided biopsy, there are some complications as in our study and as reported in literature. These complications would unfortunately become life-threatening such as sepsis or severe hemorrhage.(9) Antibiotic prophylaxis and the appropriate regimen is very important in order to avoid infectious complications.(9) In this study, we aimed to analyse the pathologic results, complications of prostate biopsies and the comparison of pathologic results with the results of radical prostatectomy.

Methods

1509 patients that were performed TRUS-guided prostate biopsy in Kecioren Research and Training Hospital between January 2008 and January 2017 were included in our study. The datas were collected retrospectively and evaluated in detail. Analyses were conducted and datas were compared with using Microsoft Excel 14.6.0 Pivot Analysis. Ages, serum PSA levels, DRE findings, infections, urine culture results, types of guide attachments and antibiotics were noted for the patients. Biopsy gleason scores, number of positive biopsy cores, positive biopsy lobes, radical prostatectomy(RP) pathology results(if available), Tumor node metastasis(TNM) classifications and RP gleason scores were recorded for the patients that were diagnosed as prostate cancer. Age-related PSA values

were used as; 0-2,5ng/ml for 0-49 years, 0-3,5ng/ml for 50-59 years, 0-4,5ng/ml for 60-69 years and 0-6,5ng/ml for 70 years and older. Abnormal DRE findings were classified as irregular firm and hard prostatic tissue and nodule palpation. The datas were analysed in detail. If the pathology results were available of RP specimens of the patients that were diagnosed as prostate cancer and were operated, they were compared with biopsy pathologies. Infections and urine culture results were also evaluated. Appropriate regimen was used in accordant with culture antibiogram results.

Biopsy technique

The patients with elevated PSA levels according to age-related PSA ranges and/or abnormal DRE findings were performed TRUS-guided prostate biopsy. Oral ciprofloxacin(750 mg), ornidazole (500 mg) and intramuscular gentamicin(single dose 80 mg) were started three days prior to biopsy date as antibiotic prophlaxis. Anticoagulants were stopped minimum 5 days prior to biopsy. BT enema was used for bowel preparation. Before the biopsy the patient was given left lateral decubitus position and local anesthetics used just before the insertion of TRUS probe. After the insertion, prilocaine was used for periprostatic nerve bloc. 12-core biopsy was performed for all patients and all the biopsy pathologies were sent to pathology department with seperate tubes. After the operation advices were given to all patients about possible complications and the urgent situations.

Results

The pathologic results of 1509 patients were evaluated in detail. The average age was 64,6 years (31-91 years). Pathologic results were examined under two categories as benign prostatic hyperplasia(BPH) and prostate cancer (PCa). 1116 patients were diagnosed as BPH and 393 patients were as PCa. The average age of BPH group was 63,7 years and it was 67,3 for PCa group. For the BPH group all PSA values were higher than the age-related PSA ranges. Average PSA level was 9,27ng/ml for BPH group. Most of the DRE findings were normal but prostate was palpated as firm and hard in 159 patients and there were nodules palpated in 181 patients. Average PSA level was 8,57ng/ml for the patients with normal DRE findings. It was 12,21ng/ml for the patients with firm and hard prostate and 9,64ng/ml for the patients that nodules were palpated. 52 patients had urinary tract infections after prostate biopsy for BPH group and 1 had severe hemorrhage. 5 types of microorganisms were isolated in urine culture. There was no microorganism in urine cultures of 28 patients. Escherischia Coli(E. Coli) was isolated in 8 patients, Expanded-spectrum beta-lactamase positive E.Coli (ESBL+E.Coli) was isolated in 12 patients. Enterococcus faecalis was isolated in 1, Klebsiella spp. was isolated in 2 and Meticillin-sensitive staphylococcus aureus was isolated in 1 (Table 1). Ciprofloxacin, imipenem, ertapenem, phophomycin+nitrofurantoin, cephtriaxone+trimetoprim, cephtriaxone+metronidazole, cephtazidime, sulperazone, imipenem+ertapenem were used as antibiotic regimens (Table 1). For the PCa group, 26 patients had infections. There was no microorganism in urine cultures of 10 patients. Escherischia Coli(E.Coli) was isolated in 3 patients, ESBL+E.Coli was isolated in 12 patients. Enterococcus faecalis was isolated in 1 (Table 1). Cephtriaxone+metronidazole, Cephtriaxone, amikacin, cefuroxime axetil, Cephtriaxone+clarithromycin were used as antibiotic regimens (Table 1). The average age of PCa group was 67,3 years. Average PSA level was 29,87ng/ml.(Table 2) PSA levels were higher than the ag-related PSA ranges and average PSA levels according to age groups were analysed (Table 2). DRE findings were normal for 173 patients. Prostate was palpated firm and hard in 133 patients and nodules were palpated in 87 patients (Table 2). Biopsy gleason (GLE) scores were classifed according to the age groups (Table 3). 134 of them were GLE 3+3, 26 were 4+3, 44 were 4+4, 2 were 5+3, 38 were 4+5, 14 were 5+4, 12 were 5+5, 14 were diagnosed as low grade prostatic intraepitelial neoplasia (LG PIN), 17 were high grade prostatic intraepitelial neoplasia (HG PIN), 42 were atypical small acinar proliferation (ASAP), 1 were HG PIN+ASAP (Table 3). The number of positive cores, gleason scores and sides of positive lobes were compared for the patients that were diagnosed as prostate cancer according to TRUS-guided prostate biopsy (Table 4). There were maximum 11 positive cores. 17 patients with maximum positive cores (11 cores) were diagnosed with GLE 4+5 PCa. Metastasis were detected in 27 patients and metastatic patients were grouped

Table 1. Infections, urine culture results and antibiotics

Infections	Culture-Antibiogram	Cephtriaxone	Ciprofloxacin	Cephtri.+trim.	Cephtri.+metronid.	Cephtazidime	Cefur. Axetil	Cephtri.+Claritro	Amikacin	Imipenem	Ertapenem	Imip.+ertap.	Phospho.+nitrofur.	Sulperazone	Total
BPH	No isolation	2	2		23							1			**28**
	E.COLI		1		7										**8**
	E.FAECALIS										1				**1**
	ESBL+ECOLİ		1		4	1				2	2		1	1	**12**
	KLEBSIELLA				2										**2**
	MSSA			1											**1**
	Total	2	4	1	36	1				2	3	1	1	1	**52**
Pca	No isolation	2			4		4								**10**
	E.COLI				3										**3**
	ESBL+ECOLİ				4			5	3						**12**
	E.FAECALIS				1										**1**
	Total	2			12		4	5	3						**26**

Table 2. Age groups, DRE findings and average PSA leves for PCa patients.

Pca	DRE				PSA
Age Groups	**Normal**	**Firm, Hard**	**Nodules**	**Total**	**Average**
30-39			1	1	98,60
40-49	4		1	5	18,55
50-59	42	14	7	63	18,72
60-69	69	56	36	161	31,22
70-79	52	55	37	144	30,34
80-89	6	7	5	18	50,58
90-99		1		1	61,00
Total	173	133	87	393	29,87

Table 3. Gleason scores according to age groups

AGE-GLE	GLE 5	GLE 3+3	GLE 3+4	GLE 4+3	GLE 4+4	GLE 5+3	GLE 4+5	GLE 5+4	GLE 5+5	LG PIN	HG PIN	ASAP	HG PIN + ASAP	TOTAL
30-39							1							1
40-49		1					1				1	2		5
50-59	1	24	3	5	4		5		2	4	3	12		63
60-69	3	54	25	14	17	1	14	5	2	3	8	14	1	161
70-79	5	51	10	6	16	1	16	7	8	6	4	14		144
80-89		4	2	1	7		1	1		1	1			18
90-99								1						1
Total	9	134	40	26	44	2	38	14	12	14	17	42	1	393

according to gleason score of prostate biopsy. 1 was GLE 5, 3 were GLE 6, 6 were GLE 7, 5 were GLE 8, 10 were GLE 9 and 2 were GLE 10. 63 of the 393 patients that were diagnosed as PCa were operated in our center or operated in another center and we were able to gain the pathology results. The results of RP were compared with prostate biopsy (Table 5). Most of the patients with lower gleason scores had PT2a and PT2c but for higher gleason scores, most of them had PT3b. There was upstaging in 7 patients with GLE 3+3. For GLE 3+4, there was downstaging for 6 patients and upstaging for 7 patients. For GLE 4+3, all the pathology results were different with biopsy. There was downstaging for 3 patients and upstaging for 2 patients. For GLE 4+4 all the gleason scores of RP were the same and there was downstaging for the patient with GLE 4+5 (Table 5). 10 of 22 patients that had left lobe positivity in prostate biopsy had positivity for both lobes according to RP and 12 had left lobe positivity. 5 of 19 patients that had right lobe positivity in prostate biopsy had positivity for both lobes according to RP and 14 had right lobe positivity. 19 of the patients that had positivity for both lobes in prostate biopsy had similar results according to RP, 2 had only right lobe positivity.

Discussion

Prostate cancer remains a big health problem in all over the world. There have been lots of studies related with the diagnosis and the treatment of prostate cancer. PSA level, digital rectal examination, transrectal ultrasonography and magnetic resonance imaging are the options that are widely used for diagnosis (10). The men with elevated PSA levels and/or abnormal digital rectal examination results undergo for prostate biopsy and none of these were undergone with normal findings so it is impossible to evaluate false-negative results (10). PSA cut-off values are different for countries and clinics. Most of the clinis use age-related ranges as in our clinic. Agnihotri et al. (11) evaluated the cut-off levels and as a result they reported that 5.4ng/ml value can be used for the patients with normal DRE findings. Pepe et al. (12) reported that the risk of prostate cancer mainly depended on the age and initial PSA level so there must be individualized approach. There is a habit of using antibacterials for lowering PSA level before deciding immediate biopsy in Turkey as in most of the other countries. Shtricker et al. (13) showed no advantage for this approach without evidence of infection. Several methods are used for prostate biopsies. Di Franco et al. (14) compared the results of transperineal (TP) prostate biopsies and transrectal biopsies (TR). The sensitivity was similar but TP biopsy detected more cancers at first time and the complication rates were lower (14). Herranz Amo et al. (15) compared the results of sextant biopsies and 10-core biopsies. There were no statistically significant diferences between these methods but more cores would be needed for larger prostates (15). Similarly Abd et al. (16) pointed the need for extra cores in patients with large prostates. Klein at al. (17) showed the superiority of 3 dimensional prostate biopsy comparing with 2 dimensional one. The necessity of repeat biopsy and the indications are still controversial. Loeb (18) mentioned the impostance of risk stratied approach and the need of individualized care. Also there has been a debate on comparison of prostate biopsy pathology results and radical prostatectomy pathology results. Arias-Stella et al. (19) compared the biopsy cleason scores and RP gleason scores. They used both composite gleason scores (CGS) and highest gleason scores (HGS). They found that CGS had lower rates for downgrading and higher prediction rates comparing with HGS (19). Hsieh et al. showed that the accuracy rate of biopsy gleason scores were 31% and they pointed that the treatment methods should not be entirely based on biopsy gleason scores (20). Ozden et al. (21) showed biopsy upgrading as almost 50% for the patients that RP was performed. There is a debate on the approach for HGPIN and ASAP detection in prostate biopsy. We prefer repeat biopsy for these cases according to serum biomarkers as the similar approach reported by Tosoian et al. (22) Most of these patients with HGPIN and/or ASAP were diagnosed as PCa after the repeat biopsies in our study. While comparing the gleason scores of prostate biopsies and radical prostatectomies in our study, we found that there were more patients that had upstaging while comparing the downstaging or same pathologies. This result clearly shows the lower accuracy rates of prostate biopsy.

The number infections after prostate biopsies have been reported as increasing in some studies (23). Fluoroqinolones are widely used for antibiotic prophlaxis (AP) for prostate biopsy as we are using a similar regimen (23). We use ciprofloxacin+gentamicin regimen for AP. The most common pathogen was found to be E.Coli as it is similar in our study (24). Despite the antibiotic regimens for prophlaxis infections would be seen due to increased number of multiresistant pathogens (23,24). Adamczyk et al. (25) recommended first or second generation of cephalosporins for fluoroquinolone-resistant E.Coli species and pointed the importance of rectal swabs

Table 4. Gleason scores, sides and number of positive cores

GLE/SIDE/+CORE	NUMBER OF POSITIVE CORES											
GLE/SIDE	1	2	3	4	5	6	7	8	9	10	11	Total
GLE 5	3	2	1		1	2						9
LEFT	2	1			1							4
RIGHT	1	1	1			1						4
RIGHT+LEFT						1						1
GLE3+3	38	37	23	9	6	9	1	4	2		5	134
LEFT	16	11	7	2	1	1						38
RIGHT	22	18	8	4		1						53
RIGHT+LEFT		8	8	3	5	7	1	4	2		5	43
GLE3+4	3	7	8	4	3	6	3	1	2		3	40
LEFT	1	6	4	1		1						13
RIGHT	2	1	3	1		1						8
RIGHT+LEFT			1	2	3	4	3	1	2		3	19
GLE4+3		2	3	4	5	4					8	26
LEFT				1								1
RIGHT		1	2	2	1	3						9
RIGHT+LEFT		1	1	1	4	1					8	16
GLE4+4	3	6	10	5	4	5	1	1		1	8	44
LEFT		1	3	1	2	2						9
RIGHT	3	3	4	2		1						13
RIGHT+LEFT		2	3	2	2	2	1	1		1	8	22
GLE4+5	1	4		1	3	5	5		1	1	17	38
LEFT		1				2						3
RIGHT	1	2			2							5
RIGHT+LEFT		1		1	1	3	5		1	1	17	30
GLE5+4		1				1		2	1		9	14
LEFT						1						1
RIGHT+LEFT		1						2	1		9	13
GLE5+5	1	1					1			1	8	12
LEFT	1											1
RIGHT+LEFT		1					1			1	8	11
LOWGR PIN	6	5	2					1				14
LEFT	1	1	1									3
RIGHT	5	2										7
RIGHT+LEFT		2	1					1				4
HIGHGR PIN	12	2	1	1							1	17
LEFT	2	2	1	1								6
RIGHT	10											10
RIGHT+LEFT											1	1
ASAP	20	18	3	1								42
LEFT	10	4										14
RIGHT	10	10	1	1								22
RIGHT+LEFT		4	2									6
ASAP+HIGHGRPIN		1										1
LEFT		1										1
GLE5+3				1		1						2
RIGHT				1		1						2
TOTAL	87	86	51	26	22	33	11	9	6	3	59	393

Table 5. **Comparison of prostate biopsy pathologies with RP.**

GLE/SIDE	NO Pathologies of RRP	GLE 3+3			GLE 3+4			GLE 4+3			GLE4+4		GLE4+5	TOTAL
	0	RIGHT	RIGHT+LEFT	LEFT	RIGHT	RIGHT+LEFT	LEFT	RIGHT	RIGHT+LEFT	LEFT	RIGHT	RIGHT+LEFT	RIGHT+LEFT	
GLE 5	9													9
LEFT	4													4
RIGHT	4													4
RIGHT+LEFT	1													1
GLE 3+3	97	9	17	4	3	1	2	1						134
LEFT	25		6	4		1	2							38
RIGHT	39	7	3		3			1						53
RIGHT+LEFT	33	2	8											43
GLE 3+4	23		3	3	1	2	1	1	1	2		2	1	40
LEFT	4		2	3		1	1			2				13
RIGHT	6				1			1						8
RIGHT+LEFT	13		1			1			1			2	1	19
GLE 4+3	21		1			2						2		26
LEFT	1													1
RIGHT	7					1						1		9
RIGHT+LEFT	13		1			1						1		16
GLE 4+4	41										1	2		44
LEFT	9													9
RIGHT	12										1			13
RIGHT+LEFT	20											2		22
GLE 5+3	2													2
RIGHT	2													2
GLE 4+5	37													38
LEFT	3													3
RIGHT	5													5
RIGHT+LEFT	29								1					30
GLE 5+4	14													14
LEFT	1													1
RIGHT+LEFT	13													13
GLE 5+5	12													12
LEFT	1													1
RIGHT+LEFT	11													11
LG PIN	14													14
LEFT	3													3
RIGHT	7													7
RIGHT+LEFT	4													4
HG PIN	17													17
LEFT	6													6
RIGHT	10													10
RIGHT+LEFT	1													1
ASAP	42													42
LEFT	14													14
RIGHT	22													22
RIGHT+LEFT	6													6
HG PIN+ASAP	1													1
LEFT	1													1
TOTAL	330	9	21	7	4	5	3	2	2	2	1	6	1	393

for determining the appropriate antibiotic (25).

The design of study was retrospective and prospective studies are necessary in order to compare different prostate biopsy techniques.

Despite the importance of TRUS-guided prostate biopsy in diagnosis of PCa, unfortunately there is not accuracy while comparing with radical prostatectomy results. Infectious complications after prostate biopsy must be carefully evaluated and antibiotic prophlaxis is critical and necessary for all patients.

Acknowledgements

The authors' responsibilities were as follows- SS: designed the research and wrote the manuscript; MY and ED: data collection and analysis, CS and OFB: revised the manuscript and statistical analysis; SS: conducted the research and had primary responsibility for the final content.

Conflict of Interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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