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Lower urinary tract symptoms and their severity in men subjected to prostate biopsy

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Introduction Lower urinary tract symptoms (LUTS) are one of most frequent complaints among men over 50 years of age. They usually result from benign prostate hyperplasia, which often coexists with cancer. The aim of the present study is to evaluate prospectively the incidence of LUTS and their character in men subjected to prostate biopsy.

Material and methods Data of men who were subjected to transrectal ultrasound guided prostate core biopsy from 1st July 2007 to 30th July 2008 in selected urological departments in Poland were analyzed. LUTS were measured with International Prostate Symptom Score (IPSS).

Results Prostate biopsy was performed in 747 men aged between 34 and 93 years (mean – 67.4; median – 68). LUTS of mild degree or no LUTS (≤7 IPSS points) were reported by 29.5% of patients. PCa was found in 60.0% of them. Among men with moderate or severe LUTS (IPSS >7 points), PCa was found in 51.4% and 55.0% of them respectively. Median PSA was 9.5 ng/ml, 9.4 ng/ml and 12.0 ng/ml in men with mild, moderate and severe LUTS respectively (NS). However, among men with severe LUTS, PCa was more likely to be less differentiated and locally advanced.

Conclusions LUTS are weak predictors of a positive result of transrectal ultrasound guided prostate biopsy. However, there is a trend to diagnose more locally advanced and less highly differentiated cancers among men with severe lower urinary tract symptoms.

Key Words: prostate ‹› lower urinary tract symptoms ‹› biopsy ‹› prostate cancer

INTRODUCTION

Prostate cancer (PCa – *prostate adenocarcinoma*) is one of the most common malignancies diagnosed in men. In 2011, PCa was found in 10,318 males living in Poland [1]. The number has almost doubled in recent years, mainly due to the introduction of prostate specific antigen (PSA) [2]. This test allows earlier recognition of the disease, long before symptoms and signs occur. Their presence is usually associated with advanced PCa. However, many practitioners believe there is a link between lower urinary tract symptoms (LUTS) and prostate cancer.

Prevalence of LUTS in senescence is high and is usually associated with benign prostate hyperplasia (BPH). More than half of men aged over 65 report moderate or severe symptoms [3, 4]. In the majority of cases, these symptoms drive urological visits followed by clinical examination and blood PSA tests. Two thirds of physicians check PSA in patients with LUTS [5]. Furthermore, 73% of men complaining of lower urinary tract symptoms express fear of cancer and are more likely to be tested for PSA [6]. Although BPH and PCa share many similarities, including dependence on age and androgens, a common pathophysiologic link remains unrecognized.

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The goal of this prospective and multicenter study is to analyze the relationship between lower urinary tract symptoms and prostate cancer in men submitted to transrectal ultrasound guided prostate biopsy (^{TRUS}tru–cut Bx).

MATERIAL AND METHODS

The data of all consecutive men subjected to ^{TRUS}tru–cut Bx from 1st of July 2007 to 30th of June 2008 in 4 Departments of Urology (Postgraduate Medical Education Center, Central Railway Hospital in Warsaw, Medical University in Warsaw, Medical Academy in Bydgoszcz, Regional Hospital named J. Biziel in Bydgoszcz) were prospectively collected and evaluated as previously described [7]. Biopsy was performed in cases of increased (^{3}4.0 ng/ml) and/or increasing PSA and/or abnormal digital recital examination (DRE) and/or abnormal transrectal ultrasound (TRUS) findings. If PSA was the only indication, so called "mapping" ^{TRUS}tru–cut Bx with sampling of 6 to 20 tissue cores was taken from different areas of the prostate – mainly the peripheral zone – and the number of cores was adjusted to the prostate volume. In cases of abnormal DRE and/or TRUS, lesion–guided biopsies were performed, usually with cores taken from other "normal" sites of the prostate in men being potential candidates for radical therapy and with a PSA of less than 10 ng/ml. In the case of prostate cancer diagnosis, its clinical stage was established by the physician performing the biopsy based upon all clinical and pathological data.

Severity of lower urinary tract symptoms was assessed with the IPSS questionnaire. Patients were divided into three groups accordingly to IPSS score: Group I ≤7 points (mild or no symptoms), Group II 8–19 points (moderate symptoms) and Group III 20–35 points (severe symptoms).

The data was collected prospectively, and a variety of clinicopathological features were compared among different groups with chi–square and Student t–tests. A test with a $p \leq 0.05$ was considered significant.

RESULTS

Prostate biopsy was done in 747 consecutive men, aged from 34 to 93 years (mean – 67.4, median – 68). Biposy indications are presented in Table 1. Most commonly, ^{TRUS}tru–cut Bx was preformed solely due to elevated PSA (46.1%). The number of men who assessed severity of their LUTS with the IPSS questionnaire was 689 (92.2%). Further analysis concerns only these men. Most of them described their complaints as moderate (48.2%). The numbers of men in subsequent groups are presented in Table 2.

Mean age did not differ significantly among different groups. However, prostate volume and PSA were lower, and PSA density (PSAD) was greater in men of Group I than in men of Groups II and III (Table 3), although the differences were significant only in comparison of Groups I and III.

Among 689 men who completed the IPSS questionnaire, prostate cancer was diagnosed in 54.7% of them. A positive result of ^{TRUS}tru–cut Bx was found most frequently in Group I; however, the difference in that respect was significant only between Groups I and II (Table 4). Simultaneously, there were no significant differences among the groups in terms of the number of cores taken during biopsy, as well as the rate of multiple biopsies done to diagnose the cancer.

Mean age of men in different groups diagnosed with cancer did not differ significantly. PSA and prostate volume were lower and PSA density was greater in men of Group I than in men of Groups II and III (Table 5).

Abnormal DRE suggestive of prostate cancer was found in 49.5% (109/220), 41.1% (148/360) and 55.1% (60/109) of men of Group I, II and III respectively. Among them, prostate cancer was diagnosed in 63.6% (84/132), 58.9%(109/185) and 76.7% (46/60) respectively.

Findings suggestive of PCa revealed by TRUS were observed in 44.5% (98/220), 29.2% (105/360) and 39.4% (43/109) of men of Group I, II and III respectively. Among them prostate cancer was diagnosed in 50.0% (66/132), 42.2% (78/185) and 50.0% (30/60) respectively.

Table 1. *Biopsy indications*

Indication	Number of subjects	Rate (%)
DRE(+) only	19	2.5
↑PSA only	344	46.1
DRE(+) and ↑PSA	149	19.9
DRE(+) and TRUS(+)	7	0.9
↑PSA and TRUS(+)	50	6.7
↑PSA and DRE(+) and TRUS(+)	178	23.8
All	747	100

Table 2. *The numbers and rates of men in Group I (≤7 IPSS points; mild or no symptoms). in Group II (8–19 IPSS points; moderate symptoms) and in Group III (20–35 IPSS points; severe symptoms)*

IPSS Groups	Number of men	Rate (%)
I	220	29.5
II	360	48.2
III	109	14.6
Not known	58	7.7
All	747	100

Table 3. *Comparison of mean age (years). PSA (ng/ml). PSAD (ng/ml/cm³) and prostate volume (Pv; cm³) in men of Group I, II and III; (p = level of significance)*

Factor	Group I			Group II			Group III			p.
	Mean	Median	Range	Mean	Median	Range	Mean	Median	Range	
Age	66.4	67	42–86	68.0	68	45–90	67.6	69	34–93	NS
PSA	12.1	8.7	1.2–74.5	37.5	9.03	0.28–2650	34.2	11.2	2.05–946.3	<0.05*
Pv	46.4	41.7	14.9–268	59.2	55	18.4–180	61.3	56.9	21–156	<0.05*
PSAD	0.48	0.19	0.02–27.2	0.95	0.16	0.01–53.2	0.55	0.155	0.05–12.5	<0.05*

* comparison among men of group I and III

Table 4. *Numbers and rates of men diagnosed with cancer in different Groups and corresponding mean numbers of cores taken during ^{TRUS}tru–cut Bx and the rates of multiple biopsies*

IPSS Groups	Mean number of cores	The rate of multiple biopsies (%)	Number of men	Rate (%)
Group I	8.8	23.2	132	60.0
Group II	9.2	30.3	185	51.4
Group III	8.7	23.9	60	55.0
All	9.0	27.0	377	100

Cancer confined to the prostate was diagnosed in 330 (87.5%) cases. It was mainly staged as T1c PCa (56.2%), (Table 6). The rate of organ confined disease was greater among men of Group I than among men of Group II and among men of Group III. The rates of cancer classified as locally advanced were 9.8%, 11.9% and 20.0% respectively.

Among 377 cases of prostate cancer Gleason score was assessed in 216 of them. Among these, Gleason score of less than 7 was most frequently found (Table 7). Again,

Table 5. *Comparison of mean age (years). PSA (ng/ml). PSAD (ng/ml/cm³) and prostate volume (Pv; cm³) in men of Group I, II and III diagnosed with prostate cancer; (p = level of significance).*

Factor	Group I			Group II			Group III			p.
	Mean	Median	Range	Mean	Median	Range	Mean	Median	Range	
Age	67.2	69	42–86	68.4	69	48–90	69.2	70	34–93	NS
PSA	14.1	9.5	1.2–74.5	59.6	9.4	1.05–2650	46.0	12.0	2.05–946.3	<0.05*
Pv	42.9	36.8	14.9–268	50.2	45.2	18.4–173	47.5	43.0	21–100	<0.05#
PSAD	0.71	0.24	0.02–27.2	0.98	0.22	0.05–53.2	1.13	0.37	0.07–12.5	<0.05*

* comparison among men of Group I and III, # comparison among men of group I and II

Table 6. *Local clinical stage of prostate cancer (cT) diagnosed in men of different groups*

Prostate cancer stage	Group I		Group II		Group III		All
	Number	Rate (%)	Number	Rate (%)	Number	Rate (%)	
T1c	62	47.0	115	62.2	35	58.3	212 (56.2%)
cT2	57	43.2	48	25.9	13	21.7	118 (31.3%)
cT ≥3	13	9.8	22	11.9	12	20.0	47 (12.5%)
All	132	100	185	100	60	100	377 (100%)

Table 7. *Gleason score of prostate cancer (Gl.s.) diagnosed in men of different groups*

Prostate cancer Gleason score	Group I		Group II		Group III		All
	Number	Rate (%)	Number	Rate (%)	Number	Rate (%)	
Gl.s. <7	48	36.4	58	31.4	14	23.3	120 (31.8%)
Gl.s. = 7	20	15.1	24	13.0	10	16.7	54 (14.2%)
Gl.s. >7	19	14.4	17	9.2	6	10.0	42 (11.1%)
Gl.s. ≥7	39	29.5	41	22.2	16	26.7	96 (25.3%)
Not known	45	34.1	86	46.4	30	50.0	161 (42.7%)
All	132	100	185	100	60	100	377 (100%)

men of Group I were less likely to be diagnosed with Gl.s. ≥7 prostate cancer than men of other groups.

DISCUSSION

We observed that among men who were qualified to prostate biopsy, cancer was found more frequently among males with moderate or severe lower urinary tract symptoms than in those with no or mild complaints. Furthermore, if PCa is diagnosed, then it tends to be locally advanced and less differentiated among men with greater IPSS scores.

It seems intuitive to state that men demonstrating indications for biopsy who present with LUTS may have their PSA elevated due to benign conditions such as BPH or prostatitis. Those who have no complaints and increased PSA may more likely be diagnosed with cancer than other diseases which usually produce symptoms and signs. This phenomenon was observed by other authors who found that in men with PSA levels between 4 and 10 ng/ml, the absence of LUTS is an independent predictor of positive results of prostate biopsy [8]. Mean prostate volume in the present study was greater among men with moderate to severe LUTS than among men without symptoms, which further confirms the causal relationship between BPH and IPSS score. The present results are in contrast to recently published data of men subjected to prostate cancer screening in Japan [9]. According to them, the presence of LUTS measured as in our study by IPSS has no influence on the subsequent diagnosis of prostate cancer. However, the number of biopsied men was 178. Among them, prostate cancer was found in only 51 cases. The authors compared two small and quite different groups of men as the number is considered: 34 with mild and 17 with moderate to severe LUTS. Mean prostate volume amounted to 21.8 ml and mean age was 70.4 years. During biopsy, only 6 cores were taken. Although not relevant in our analysis, it is observed that LUTS drive the patients to visit their physicians, so males complaining on the lower urinary tract symptoms are more prone to be subjected to prostate biopsy and subsequent cancer diagnosis as opposed to those without any complaints [10].

Interestingly, our results indicate that men with severe LUTS and prostate cancer diagnosis are more likely to have locally advanced disease than men with mild symptoms. It was previously shown by Meigs et al that among men with elevated PSA (>4 ng/ml), those with mild LUTS are about twofold more likely to be diagnosed with organ confined prostate cancer than men with moderate to severe symptoms [11]. Most patients in the present study with severe LUTS who were found to have prostate cancer, were also found to have abnormal DRE and TRUS despite elevated PSA. These may suggest the presence of cancer which has substantial burden and therefore may influence the presence of symptoms. We have previously noted that T1c PCa has more favorable oncological characteristics than one that is felt or visible [12]. The mean and median levels of PSA were greatest in those with severe LUTS. It was confirmed that the greater the PSA, the higher the rate of locally advanced disease.

This study has several drawbacks. The data was collected from selected groups of patients. They were qualified for biopsy by different urologists in four different centers and do not represent the general population as men with low PSA levels, normal DRE and TRUS. Furthermore, the biopsy templates were not homogenous among different centers and the numbers of cores taken during the biopsies was not strictly comparable.

CONCLUSIONS

Lower urinary tract symptoms are weak predictors of positive results of transrectal ultrasound guided prostate core biopsy because the difference was only significant between the group of men with no or mild symptoms and those with moderate LUTS. Although the rate of unfavorable biopsy results was greater in men with severe symptoms than in those without complaints, the difference did not reach the level of significance. When cancer is diagnosed, it tends to be more advanced and less well differentiated in the group of men with significant LUTS.

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