Urological Oncology

Are Men Who Undergo Radical Prostatectomy with Lower Urinary Tract Symptoms at an Increased Risk for Aggressive Prostate Cancer?

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**Purpose:** We aimed to determine whether prediagnostic lower urinary tract symptoms (LUTS) are associated with the aggressiveness of nonmetastatic prostate cancer (PCa) and compared the clinicopathologic features of PCa patients with and without preexisting LUTS.

**Materials and Methods:** We retrospectively reviewed the medical records of 295 prostate cancer patients who underwent a radical prostatectomy (RP) by a single surgeon from 2006 to 2010. A total of 205 patients were assigned to two groups according to whether they showed preoperative LUTS (International Prostate Symptom Score [IPSS] ≥ 8). Clinical, operative, pathologic, and postoperative functional data were collected.

**Results:** The mean age at RP was 62.7 years in the no LUTS group (group A, n=108) and 64.7 in the LUTS group (group B, n=97). The baseline mean IPSS score was 6.1 in group A and 14.6 in group B (p=0.029). The incidence of pathologic T3a stage or above was significantly higher in group B than in group A (p=0.036). The mean postoperative follow-up period was 16.8 months (range, 4 to 38 months). The mean time to biochemical recurrence was 16.9 and 18.2 months in groups A and B, respectively (p=0.148). The median time to recovery of urinary incontinence was 3.6 and 3.3 months in groups A and B, respectively.

**Conclusions:** PCa patients without baseline LUTS had a favorable result of pathologic T stage even though there were no significant differences in biochemical recurrence or recovery of postoperative incontinence compared with patients with baseline LUTS.

**Key Words:** Prostatectomy; Prostatic hyperplasia; Prostatic neoplasms

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**INTRODUCTION**

Generally, serum prostate-specific antigen (PSA) testing in clinical practice is used either in the screening of asymptomatic men or in the workup of men with lower urinary tract symptoms (LUTS). Although an elevated PSA level can be an important predictor of prostate cancer (PCa), it may also be indicative of benign prostatic hyperplasia. Several studies have reported a weak association between LUTS and the detection of PCa [1,2]. Men with LUTS are often concerned that their symptoms indicate PCa [3]. They believe the PSA evaluation to be more effective for the detection of PCa than do men who have not been tested [4]. PSA, Gleason score at biopsy, and clinical stage are currently the most reliable markers of aggressiveness or prognosis for PCa [3]. However, controversy exists regarding whether prediagnostic LUTS affects the aggressiveness of PCa [1,5]. Collin et al reported that associations of LUTS with PCa did not differ between localized or advanced PCa [1]. In our study, we aimed to determine whether prediagnostic LUTS are associated with the aggressiveness of nonmetastatic PCa and compared the clinicopathologic
features of PCa patients with and without preexisting LUTS.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 295 prostate cancer patients who underwent a radical prostatectomy (RP) by a single surgeon from 2006 to 2010. In our study, prostate cancer diagnosis took one of the following two main routes: asymptomatic diagnosis following a screening test or symptomatic diagnosis with LUTS. All patients attended the center’s urology department at the initial visit for completion of an International Prostate Symptom Score (IPSS) questionnaire, digital rectal examination, PSA test, and transrectal ultrasound (TRUS) (12 cores). We defined the LUTS group as those with IPSS ≥ 8 and the no LUTS group as those with IPSS < 8.

After excluding those patients with unclear medical records, a history of medication with an alpha blocker or 5 alpha reductase inhibitor, a history of prostate surgery, clinical and the no LUTS group as those with IPSS < 8. The mean age at RP was 62.7 years in the no LUTS group (group A, n=108) and 64.7 years in the LUTS group (group B, n=97). Other preoperative baseline parameters such as past history, body mass index, and clinical stage were not statistically different between the two groups. The baseline mean IPSS score was 6.1 in group A and 14.6 in group B (p=0.029), and the mean quality of life score was 2.6 in group A and 4.2 in group B (p=0.013). There was no significant difference in preoperative prostate-specific antigen levels (10.1 vs. 11.2 ng/ml in groups A and B, respectively) (Table 1). The prostate volume was large in the LUTS group (39.8 cc) compared with the no LUTS group (34.5 cc); however, there was no significant difference between the two groups.

The incidence of a pathologic stage of T3a or above was significantly higher in group B than in group A (p=0.036). After RP, the incidence of Gleason scores of 7 or more was 69 (64.8%) and 59 (60.9%) in groups A and B, respectively. The incidence of a positive surgical margin showed no significant difference between the two groups (Table 2). In the multivariate analysis, IPSS total scores and biopsy Gleason scores were predictable values for locally advanced PCa (Table 3).

The mean postoperative follow-up period was 16.8 months (range, 4 to 38 months) (Table 2). We used the Kaplan-Meier analysis to compare the biochemical recurrence rate between the two groups (Fig. 1). The mean time to biochemical recurrence was 16.9 and 18.2 months in groups A and B, respectively (p=0.148). The median time to recovery of urinary incontinence was 3.6 and 3.3 months in groups A and B, respectively. This result did not differ significantly between the two groups.

DISCUSSION

In the present study, more than half (52.7%) of the men with no baseline LUTS were diagnosed with PCa and underwent RP. In addition, we demonstrated that the group with no LUTS at baseline had a favorable pathologic stage (< T2) of PCa after RP compared with the LUTS group, even though this result did not affect the biochemical recurrence rate. However, there was no evidence of a positive association with advanced PCa, which was partially contradictory to our results. Because most PCa develops in the peripheral
Effects of Preoperative LUTS on Aggressiveness of Prostate Cancer

### TABLE 1. Preoperative clinical tumor characteristics of prostate cancer patients

| Variables                  | No LUTS group (n=108) | LUTS group (n=97) | p-value |
|----------------------------|-----------------------|------------------|---------|
| Mean age (yr)              | 62.7±5.3 (49-71)      | 64.7±4.9 (51-74) | 0.314   |
| Prostate volume (cc)       | 34.5±2.9 (16-52)      | 39.8±3.2 (19-79) | 0.085   |
| Preoperative PSA (nl/ml)a   | 10.1±0.8 (3.5-19.8)   | 11.2±0.9 (3.1-21.7) | 0.612 |
| IPSS total score (mean)a    | 6.1±0.5 (0-7)        | 14.6±1.2 (9-35)  | 0.029   |
| QoL scores (mean)a         | 2.6±0.2 (0-4)        | 4.2±0.3 (2-6)    | 0.013   |
| ≤6 (%)                     | 3 (2.8)              | 6 (6.2)          | 0.222   |
| ≥7 (%)                     | 31 (28.7)            | 36 (37.1)        |         |
| ≥8 (%)                     | 74 (68.5)            | 55 (56.7)        |         |
| Clinical T stage (N)b      |                       |                  | 0.192   |
| ≤T2 (%)                    | 76 (70.4)            | 63 (64.9)        |         |
| ≥T3 (%)                    | 32 (29.6)            | 34 (35.1)        |         |

The values in parentheses for age, prostate volume, preoperative PSA, and PSA density are ranges, LUTS: lower urinary tract symptoms, PSA: prostate-specific antigen, IPSS: international prostate symptom score, QoL: quality of life. a: student’s t-test, b: pearson chi-square test

### TABLE 2. Pathological findings from analyses of prostatectomy specimens according to preoperative LUTS

| No LUTS group (n=108) | LUTS group (n=97) | p-value |
|-----------------------|-------------------|---------|
| Postoperative Gleason score |                    | p=0.193 |
| ≤6 (%)                | 39 (36.1)         | 33 (34.0) |         |
| 7 (%)                 | 60 (55.5)         | 45 (46.4) |         |
| ≥8 (%)                | 9 (8.3)           | 14 (14.5) |         |
| Postoperative pathologic stage (%) | | p=0.036 |
| T1-T2 (%)            | 82 (75.9)         | 59 (60.8) |         |
| ≥T3 (%)              | 26 (24.1)         | 38 (39.2) |         |
| Positive surgical margins (N) | | p=0.151 |
| No (%)                | 16 (14.8)         | 13 (13.4) |         |
| Yes (%)               | 87 (80.6)         | 79 (81.4) |         |
| Mean duration to biochemical recurrence (mo)b | 16.9±1.5 (6-36) | 17.2±1.6 (8-48) | p=0.158 |

LUTS: lower urinary tract symptoms, a: pearson chi-square test, b: student’s t-test

zone of the prostate and needs to be advanced before provoking LUTS, a positive association with advanced cancer would be expected if such cancers truly caused LUTS. Our results indicate that the prospect of benefit outweighs the potential for harm and that screening for early PCs is worthwhile even though the value of population-based screening has to be demonstrated in well-conducted randomized trials.

There is a widespread misconception that the risk of PCs is increased with the severity of LUTS, but a lack of cancer symptoms does not mean that there is no cancer. Catalona et al found that the absence of prostatic disease symptoms is more predictive of cancer than their presence [10]. In addition, there are many reports that patients with baseline LUTS are not at higher risk for PCs than are asymptomatic men [1,8,11]. Especially, men with a PSA level of ≥3 ng/ml and LUTS were more likely to be diagnosed with benign disease than with PCs [1]. However, the present study included only patients treated with RP, and the data therefore give no information about patients referred to the department with or without symptoms who did not have a diagnosis of PCs or any nonsurgical treatment thereof. Our results warrant future study to determine the “pure” incidence of prostate cancer in the screened population of Korea.

In the present study, there were no significant differences in postoperative Gleason scores, biochemical recurrence, or positive surgical margins, regardless of the
FIG. 1. Kaplan-Meier analysis of time to biochemical recurrence (A) and recovery of continence (B) for patients with and without baseline lower urinary tract symptoms. BCR: biochemical recurrence, IPSS: international prostate symptom score.

presence or absence of baseline LUTS. This finding is important, because measurement of PSA when a patient has LUTS is controversial. Regardless of the PCa detection rate according to baseline LUTS, our results suggest that there might be more aggressive pathologic features in the no LUTS group if the subjects had not participated in PCa screening. Some authors insist that PSA testing in men with LUTS should be standard procedure, whereas others believe it is the equivalent of screening and therefore inappropriate [12,13]. The incidence of PCa has rapidly increased over the past 10 years in East Asia, including Korea [14,15]. In South Korea, PSA screening is not yet recommended in the national early detection strategy for cancer, even though a growing proportion of patients undergoing RP are asymptomatic and are diagnosed as a result of unsystematic PSA screening. In a 2004 telephone survey of over 700 Korean men older than 50 years in a small city, approximately 15% had been screened for PCa during the previous 2 years (unpublished data), a much lower rate than the 75% reported for men in the United States [16].

In view of the growing proportion of asymptomatic PCa, we suggest that PSA screening is needed not only in men with LUTS that could be caused by PCa, but also in men who are asymptomatic at baseline [17,18].

There are several limitations to our study. First, the short duration with a relatively small number of patients requires further investigation for a longer period of time with a larger number of patients. In fact, we could not explain the exact background by which the correlation between low IPSS and low T stage was made. We think this will be an important point to clarify in future studies. Also, we were unable to include advanced or metastatic PCa cases because only RP patients were included in our study. Therefore, this study cannot assess the relationship between LUTS and more advanced or metastatic PCa.

CONCLUSIONS

PCa patients without baseline LUTS had a favorable result of pathologic T stage even though there were no significant differences in biochemical recurrence or recovery of postoperative incontinence compared with patients with baseline LUTS.

Conflicts of Interest

The authors have nothing to disclose.

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