CLINICAL STUDY

Active surveillance or radical prostatectomy? Which treatment is best?

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ABSTRACT

OBJECTIVE: We evaluated the patients who are candidates for active surveillance and treated with radical prostatectomy. These patients were compared with other patients who had not met the criteria of active surveillance.

METHODS: In total, 135 patients were included in the study. The patients were divided into two groups. The patients in Group 1 had less than three positive cores, Gleason 6 (3 + 3) and PSA level equal to or less than 10 ng/ml. Patients in Group 2 had three or more positive cores, Gleason 6 (3 + 3) and PSA level equal to or higher than 10 ng/ml. Pathological results of each groups were compared.

RESULTS: The patients' ages were between 52 and 76, and 50 and 77 in groups 1 and 2, respectively. There were 69 and 66 patients in groups 1 and 2, respectively. The mean age of patients, PSA levels, PSA density, and prostate volumes were 63.89 ± 5.89 years, 5.82 ± 1.84 ng/ml, 0.14 ± 0.07 and 51.21 ± 31.75 cc (Group 1) and 65.77 ± 6.36 years, 13.65 ± 17.11 ng/ml, 0.63 ± 1.03 and 45.44 ± 26.77 cc (Group 2). T2a, T2c, T3a and T3b were reported in 28 patients, 36 patients, 3 patients and 2 patients after pathological evaluation in Group 1, respectively. T2a, T2c, T3a and T3b were reported in 13 patients, 47 patients, 5 patients and 1 patient in the other group, respectively.

CONCLUSION: The final pathology showed that there is no difference in the positive surgical margin, proportion of insignificant prostate cancer and Gleason upgrading between groups. The clinicians must be aware of the fact that active surveillance can be misdiagnosed in some patients (Tab. 2, Ref. 20). Text in PDF www.elis.sk.

KEY WORDS: prostate cancer, cancer-specific death, prostate specific antigen, PSA testing retropubic prostatectomy.

Introduction

Prostate cancer (PCa) is the most common noncutaneous cancer and the second leading cause of cancer death among men in Western countries (1). The widespread use of prostate-specific antigen (PSA) screening and ultrasound-guided prostate biopsy protocols have increased the proportion of patients at low-risk for PCa (2). However, 75% of the patients have non-palpable tumors, and only 5% have metastasis at the time of the diagnosis (1). Tumor volume in single positive core may be small and these tumors are expected to be insignificant PCa (3). Many of these patients have insignificant PCa (IPCa) characterized by low volume, early stage and are well differentiated (low Gleason score) making them candidates for active surveillance (AS) or watchful waiting (1). Radical prostatectomy (RP) is a curative treatment for localized PCa, especially in low-risk PCa patients but RP is an overtreatment considering the morbidities, oncologic features and postoperative complications in these patients with IPCa (2).

Epstein criteria are the most common used set of definitions for determining whether PCa is significant or not and these criteria are the basis for AS (4). Epstein criteria are as follows: PSA density of less than 0.15 ng/dl, Gleason score ≤ 6, less than 3 positive cores, and < 50% of cancer involvement in any core (5). Clinically insignificant PCa was defined by Epstein and Walsh as follows: low volume tumor (≤ 0.5 ml), Gleason ≤ 6, and organ-confined disease in radical prostatectomy specimens (6).

We aimed to evaluate the clinical importance and pathological results in patients who are candidates for AS and compared them with those of other patients.

Materials and methods

One hundred and eighty-one patients who underwent open radical prostatectomy between January 2004 and January 2013 were enrolled. We extracted the patients who were diagnosed with less than 3 positive cores, PSA level ≤ 10 ng/dl, and cancer involvement of < 50% in cores with Gleason score 6 for Group 1. The patients who had more than two positive cores and or PSA levels > 10 ng/dl with Gleason score 6 were included in Group 2. Transrectal ultrasound-guided prostate biopsies were done in lateral decubitus position. Biopsies were taken with an automatic biopsy gun with 18-gauge cutting biopsy needle. The prostate
cores consist of the area of the base, mid and apex in sextant protocols. The 8 core protocol includes transition zone on each lobe. Twelve core biopsies included an additional 3 cores from the peripheral zones more laterally on each side. PSA levels, and prostate biopsy results were recorded. Prostatectomy specimens were weighted and PSA density was calculated by dividing the PSA by the weight of the prostate.

The tumor was graded according to the Gleason scoring system and staged using TNM classification. Clinically, IPCa was defined by Epstein criteria. These criteria are tumor volume ≤ 0.5 cc, Gleason score ≤ 6, and organ-confined disease. Statistical analyses were performed by SPSS, and ANOVA was used for statistical difference (p < 0.05).

Results

The characteristics of the patients (groups 1 and 2) are shown in Table 1. Seventeen patients presented a single limited adenocarcinoma at biopsy, 41 patients had a single positive core, and 28 patients had two positive cores in group 1. Among the patients, positive core localizations on apex, mid, transition and base were in 32, 27, 21 and 17 patients, respectively. Five patients had prior prostate biopsy while 4 of them were diagnosed with benign prostatic hyperplasia and 1 patient with atypical small acinar proliferation.

Of the 66 patients in group 2, 7 patients presented with limited adenocarcinoma at prostate biopsy. Eighteen patients had a single positive core, 6 patients had two positive cores, and 42 patients had more than 2 positive cores. Prior prostate biopsies were done in 4 patients of whom 1 was diagnosed with benign prostate hyperplasia and 3 with atypical small acinar proliferation.

After the radical prostatectomy, Gleason score was upgraded to 7 (3 + 4 and 4 + 3) and 8 (4 + 4) in 16 and 2 patients, respectively, and downgraded to 5 (3 + 2) in only one patient in group 1. IPCa were present in 9 patients (13 %). Positive surgical margin (PSM) was present in 6 patients; at apex in 4 patients, at base in 1 patient, at apex and base in 1 patient. Stage T2a, T2b, T2c and T3a were reported in 28 patients, 36 patients, 3 patients and 2 patients, respectively in Group 1. In Group 2, Gleason score was upgraded to 7 (3 + 4 and 4 + 3) in 24 patients and was downgraded to 5 (3 + 2) in one patient. Finally, 4 of 66 patients (6 %) met the criteria of IPCa and 13, 47, 5 and 1 patient were classified as T2a, T2c, T3a and T3b, respectively. Positive surgical margin was reported in 5 patients; 4 were at apex and one was at base (Tab. 2). There was no statistically significant difference between groups for IPCa, PSM, Gleason score, and T stage at final pathology.

Discussion

Prostate cancer staging and grade migration have led to a significant decrease in locally advanced disease in patients in the last decade (7). As a result, small focus of well-differentiated PCa in one single core of biopsy rate has increased (2). These cancers inflict little harm to the patient during his lifetime, while overdiagnosis leads potentially to overtreatment which is reported to be around 40-50 % in the European Screening Program (8). They reported that 43 % of the study population undergoing RP had minimal cancer and an estimated 1,410 men needed to be screened with 48 radical prostatectomies performed for preventing a single death in the European Randomized Study of Screening for Prostate Cancer (9). Watchful waiting (WW) and active surveillance (AS) were defined to reduce overtreatment. The most commonly used criteria of insignificant prostate cancer (IPCa) are based on the pathologic assessment of radical prostatectomy specimen (5). There are three well-established prognostic factors: Gleason score ≤ 6, organ-confined disease, and tumor volume < 0.5 cm³. The reported risk of IPCa on radical prostatectomy specimens after such a diagnosis has varied in the literature (10). Allan et al (11) reported that most patients with limited tumor (≤ 0.5 mm in extent) have had IPCa, while only 33 % of the patients had tumors warranting definitive therapy at final pathology. On the contrary, Boccon Gibod et al (2) evaluated the patients with a single focus of 3 mm or less in length at biopsy with Gleason score ≤ 6, and only 29 % of the patients met the criteria of IPCa. DiMarco et al (12), and Lee et al (13), reported that the percentage of IPCa in radical prostatectomy specimens was 28–25.3 % in the patients with Gleason 6. We found that 13 % of the patients with less than 3 positive cores, Gleason score 6, and PSA level ≤ 10 ng/ml had IPCa and the overall percentage of IPCa was 9.6 % at radical prostatectomy specimens in the current study.

Active surveillance protocol has some criteria but the centers use different selection criteria based on Gleason score, cancer extent on biopsy, and PSA levels (14). In general, criteria are stage
T1c/T2a, PSA < 10 ng/ml, and prostate biopsy Gleason ≤ 6 in three or fewer cores with ≤ 50 % involvement (15). We used these criteria with less than 3 cores for AS protocol (13). Active surveillance (AS) is a viable option of close monitoring for low-risk prostate cancer patients with regular follow-up for PSA, prostate biopsy, and digital rectal examination (9). AS protocol includes: PSA testing (every 3–4 months), digital rectal examination (every 3–6 months), transrectal ultrasonography (every 9–12 months) and prostate biopsy (after 12 years, then every 1–2 years if indicated by PSA or other examinations; 16). In a review of Dall’Era et al (16), out of the patients who were treated by AS, 14–35 % were treated because of disease progression in the follow-up period for more than 40 months.

The incidence of upgrading, Gleason score 6 (3 + 3) to ≥ 7 at radical prostatectomy specimens is a mean of 36 % and a median of 35.5 % (range 14–51 %) in literature (12). Samaratunga et al (10) reported the incidence of upgrading the patients with 0.5 mm focus or less of GS 6 on needle biopsy to be 31.8. PSA levels, pathology weight, age, extent of cancer on biopsy and needle biopsy sampling can affect the incidence of upgrading (17). Louis et al (15), reported that 41.5–1 % of the patients in the low risk group (PSA < 10 ng/ml and biopsy Gleason ≤ 6) upgraded to 7 and ≥ 8. In another study from Canada, retrospective study of 728 patients diagnosed with Gleason 6 and treated with radical prostatectomy, 49.6 % of the tumors were upgraded to 7 (18). In our study, the incidence of upgrading all patients was 30.3 % (26% in Group 1, and 34.8 % in Group 2; p = 0.421). Interestingly, Gleason 8 was found in two patients from active surveillance group.

Regarding the pathological stage, Walker et al (18), reported that 80.8 % of the patients who were diagnosed with Gleason 6 preoperatively had pT2 tumors and 19.2 % of the patients were pT3. Samaratunga et al (10) analyzed 58 patients with a single minute focus of GS 6 and reported that 48 (82.75 %) had stage pT2, and 8 (13.8 %) had stage pT3. In another study from Brazil, 87.9 % of the patients with a single positive core of GS ≤ 6 had stage pT2 and 12.1 % had stage pT3 (1). We found similar results in this study. Out of all patients, 124 patients (91.8 %) had pT2 and 11 patients (8.1 %) had pT3. The pT2 and pT3 incidences are 92.7 % and 7.2 %, respectively, in the patients in Group 1, and 90.9 % and 9.1 %, respectively in the patients in Group 2.

Positive surgical margin (PSM) means the presence of cancer at the linked resection margin of radical prostatectomy specimens (19). The prognostic impact of PSMs on outcomes after radical prostatectomy is still unclear. The incidence of PSMs ranged from 6 % to 41 % after radical prostatectomy. The apex is a frequent location of PSMs; the authors have argued that many apical PSMs were artefactual (20). Posterolateral PSM is associated with incomplete cancer resection. Surgical margin rates were attributed to several factors such as pathological stage and grade, cancer volume and location, surgical technique, lymph node involvement, specimen processing, and pathological examination. PSMs were present in 11 (8 %) patient while 10 of the patients had stage pT2 and 4 patients had GS 7 (3 + 4 or 4 + 3).

Conclusion

There is no clear consensus about the predictive operation in patients who had insignificant prostate cancer or favorable results from radical prostatectomy specimens. The patients who are candidates for active surveillance are likely to have a clinically significant carcinoma; only a small group of the patients had insignificant prostate cancer at final pathology. Positive surgical margin and Gleason score upgrading are other risk factors in these patients.

References

1. Silva RK, Dall’Oglio MF, Sant’ana AC, Junior JP, Srourgi M. Can Single Positive Core Prostate Cancer at biopsy be Considered a Low-Risk Disease after Radical Prostatectomy? Int Braz J Urol 2013; 39: 800–807.

2. Boccon-Gibod LM, Dumonceau O, Toublanc M, Ravery V, Boccon-Gibod LA. Micro-Focal Prostate Cancer: A comparison of Biopsy and Radical Prostatectomy Specimen Features. Eur Urol 2005; 48: 895–899.

3. Ahn HJ, Ko YH, Jang HA, Kang SG, Kang SH, Park HS, Lee JG, Kim JJ, Cheon J. Single Positive Core Prostate Cancer in a 12-Core Transectal Biopsy Scheme: Clinicopathological Implications Compared with Multifocal Counterpart. Korean J Urol 2010; 51: 671–676.

4. Yeom CD, Lee SH, Park KK, Park SU, Chung BH. Are Clinically Insignificant Prostate Cancers Really Insignificant among Korean Men. Yonsei Med J 2012; 53: 358–362.

5. Ploussard G, Epstein JJ, Montironi R, Carroll PR, Wirth M, Grimm MO, Bjartell AS, Montorsi F, Freedland SJ, Erbersdobler A, Kwast TH. The Contemporary of Significant Versus Insignificant Prostate Cancer. Eur Urol 2011; 60: 291–303.

6. Montanari A, Nero AD, Gazzano G, Mangiariotti B, Bernardini P, Longo F, Cordima G, Itri E. Minute focus of prostate cancer on needle biopsy: Correlation with radical prostatectomy specimen. Arch Ital Urol Androl 2009; 81: 9–12.

7. Gallina A, Maccagnano C, Squardi N, Capitano U, Abdollah F, Raber M, Salonia A, Scattoni V, Rigatti P, Montorsi F, Briganti A. Unilateral positive biopsies in low risk prostate cancer patients diagnosed with extended transrectal ultrasound-guided biopsy schemes do not predict unilateral prostate cancer at radical prostatectomy. BJU International 2011.

8. Draisma G, Boer R, Otto SJ, Can Der Crijnsen IW, Damhuis RAM, Schroder FH et al. Lead times and overdection due to prostate specific antigen screening: estimates from the European randomized study of screening for prostate cancer. J Nat Cancer Ins 2003; 95: 868–878.

9. Oon SF, Watson RW, O’Leary JJ, Fitzpatrick JM. Epstein criteria for insignificant prostate cancer. BJU International 2011; 8: 518–525.

10. Samaratunga H, Yaxley J, Kerr K, McClymont K, Duffy D. Significance of Minute Focus of Adenocarcinoma on Prostate Needle Biopsy. Urology 2007; 70: 299–302.

11. Allan RW, Sanderson H, Epstein JJ. Correlation of minute (0.5 mm or less) focus of prostate adenocarcinoma on needle biopsy with radical prostatectomy specimen: role of prostate specific antigen density. J Urol 2003; 170: 370–372.

12. DiMarco DS, Blue ML, Zincke H et al. Multivariate models to predict clinically important outcomes at prostatectomy for patients with organ-confined disease and needle biopsy of Gleason scores of 6 or less. Urol Oncol 2003; 21: 439–446.
13. Lee MC, Dong F, Stephenson AJ, Jones JS, Magi-Galluzzi C, Klein EA. The Epstein criteria predict for organ-confined but not insignificant disease and a high likelihood of cure at radical prostatectomy. Eur Urol 2010; 58: 90–95.

14. Bratt A, Carlson S, Holmberg E, Holmberg L, Johansson E, Johansson A et al. The study of Active Monitoring in Sweden (SAMS): A randomized study comparing two different follow-up schedules for active surveillance of low risk prostate cancer. Scand J Urol 2013; 47: 347–355.

15. Louis AS, Kalnin R, Maganti M, Pintilie M, Matthew AG, Finelli A. Oncologica outcomes following radical prostatectomy in the active surveillance era. CUAJ 2013; 7: 475–480.

16. Dall’Era MA, Cooperberg MR, Chan JM, Davies BJ, Albertsen PC, Klotz LH. Active Surveillance for Early-stage Prostate Cancer. Cancer 2008; 112: 1650–1659.

17. Epstein JI, Feng Z, Trock BJ, Pierorazio PM. Upgrading and Downgrading of Prostate Cancer from Biopsy to Radical Prostatectomy: Incidence and Predictive Factors Using the Modified Gleason Grading System and Factoring in Tertiary Grades. Eur Urol 2012; 61: 1019–1024.

18. Walker R, Lindner U, Louis A, Kalnin R, Ennis M, Nesbitt M et al. Concordance between transrectal ultrasound guided biopsy results and radical prostatectomy final pathology: Are we getting better at predicting final pathology? CUAJ 2014; 8: 47–52.

19. Alkhateeb S, Alibhai S, Fleshner N, Finelli A, Jewett M, Zlotta A, Nesbitt M, Lockwood G, Trachtenberg J. Impact of Positive Surgical Margins After Radical Prostatectomy Differs by Disease Risk Group. J Urol 2010; 183: 145–150.

20. Stephenson AJ, Wood DP, Kattan MW, Klein EA, Scardino PT, Eastham JA, Carver BS. Location, Extent and Number of Positive Surgical Margins Do Not Improve Accuracy of Predicting Prostate Cancer Recurrence After Radical Prostatectomy. J Urol 2009; 182: 1357–1363.

Received February 2, 2016.
Accepted February 16, 2016.