Kaohsiung Journal of Medical Sciences (2018) 34, 385–390

Available online at www.sciencedirect.com

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journal homepage: http://www.kjms-online.com

Original Article

Effects of perineural invasion in prostate needle biopsy on tumor grade and biochemical recurrence rates after radical prostatectomy

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Received 12 June 2017; accepted 28 December 2017
Available online 20 January 2018

KEYWORDS
Biochemical recurrence (BR);
Extraprostatic extension;
Perineural invasion (PNI);
Prostate cancer;
Recurrence-free survival (RFS)

Abstract To predict local invasive disease before retropubic radical prostatectomy (RRP), the correlation of perineural invasion (PNI) on prostate needle biopsy (PNB) and RRP pathology data and the effect of PNI on biochemical recurrence (BR) were researched. For patients with RRP performed between 2005 and 2014, predictive and pathologic prognostic factors were assessed. Initially all and D'Amico intermediate-risk group patients were comparatively assessed in terms of being T2 or T3 stage on RRP pathology, positive or negative for PNI presence on PNB and positive or negative BR situation. Additionally the effect of PNI presence on recurrence-free survival (RFS) rate was investigated. When all patients are investigated, multivariate analysis observed that in T3 patients PSA, PNB Gleason score (GS) and tumor percentage were significantly higher; in PNI positive patients PNB GS, core number and tumor percentage were significantly higher and in BR positive patients PNB PNI positivity and core number were significantly higher compared to T2, PNI negative and BR negative patients, separately ($p < 0.05$). When D'Amico intermediate-risk patients are evaluated, for T3 patients PSA and PNB tumor percentage; for PNI positive patients PNB core number and tumor percentage; and for BR positive patients PNB PNI positivity were significantly higher compared to T2, PNI negative and BR negative patients, separately ($p < 0.05$). Mean RFS in the whole patient group was 56.4 ± 4.2 months for PNI positive and 96.1 ± 5.7 months for negative groups. In the intermediate-risk group, mean RFS was 53.7 ± 5.1 months for PNI positive and 100.3 ± 7.7 months for negative groups ($p < 0.001$). PNI positivity on PNB was shown to be an important predictive factor for increased T3 disease and BR rates and reduced RFS.

Conflicts of interest:All authors declare no conflicts of interest.

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https://doi.org/10.1016/j.kjms.2017.12.014
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Introduction

For localized prostate cancer treatment, the aim of retropubic radical prostatectomy (RRP) is to cure prostate cancer. In localized prostate cancer patients, extraprostatic extension, seminal vesicle invasion and lymph node metastasis comprise local distribution findings on pathology after RRP [1,2]. To predict local invasion and disease recurrence before treatment, many nomograms and risk classifications have been developed [1–6]. One of the most referred classifications is the D'Amico risk classification. According to D'Amico risk classification, localized prostate cancer is investigated in 3 groups. These are low-risk, intermediate-risk and high-risk group prostate cancers [5]. The intermediate-risk group is divided into two subgroups in some studies as low-volume and high-volume intermediate-risk groups [7]. In active surveillance studies, generally low-risk group prostate cancer and low-volume intermediate-risk group prostate cancer patients are included together [8,9].

Extension of prostate cancer cells along the nerve bundle is reported as perineural invasion (PNI) on prostate pathology [10]. PNI is reported in 20% of biopsy material with prostate adenocarcinoma identified [7]. The presence of PNI is generally accompanied by high Gleason score (GS) and high prostate specific antigen (PSA) rates [7]. Additionally, some studies have shown a correlation between PNI presence and extraprostatic extension and surgical margin positivity [7,11,12]. However, PNI presence has not been included as a parameter in any studies predicting local invasion.

In this study, PNI positivity on prostate needle biopsy (PNB) in all patients and intermediate-risk group patients according to D'Amico risk classification, the correlation of PNI with other preoperative factors and effect on postoperative data was analyzed in 380 patients with RRP performed for prostate adenocarcinoma at our clinic.

Methods

PSA, PNB and RRP pathology data of the male patients with RRP performed between 2005 and 2014 were retrospectively assessed. Patients were first divided into two groups with RRP pathology stage T2 or T3, then as two groups with PNI positive or negative on PNB pathology and lastly in two groups as positive or negative for BR. First all patients and then D'Amico intermediate-risk group patients were assessed in these groups. In the groups, preoperative factors such as PSA, PSA density (PSA/prostate volume measured transrectally), PNB pathology data (GS, core number, tumor percentage and PNI presence) and level of D'Amico risk classification were evaluated. According to D'Amico risk classification, patients with PSA $<$ 10 ng/ml and PNB GS $\leq$ 6 and clinical stage T1c-T2a are in the low-risk group; patients with PSA 10–20 ng/ml and/or PNB GS $=$ 7 and/or clinical stage T2b are in the intermediate-risk group; and patients with PSA $>$20 ng/ml and/or PNB GS $\geq$ 8 and/or clinical stage T2c are in the high-risk group. Postoperative data including RRP pathology data (GS, tumor volume, tertiary Gleason pattern, surgical margin positivity and lymph node metastasis) and follow-up BR rates were investigated. After all patients were evaluated, intermediate-risk group patients were separately evaluated. This evaluation also investigated patient rates abiding by active surveillance criteria (PSA $\leq$ 10 ng/ml, PNB GS $\leq 3+4=7$, core number $\leq$ 2, tumor percentage $\leq$ 50% and clinical stage $\leq$ T2a), in other words low-volume intermediate-risk patients and patients not abiding by these criteria, or high-volume intermediate-risk patients.

Statistical analysis

Firstly preoperative data of all patients, then of D'Amico intermediate-risk patients, was comparatively evaluated between T2 and T3 groups, between PNI positive and negative groups and between BR positive and negative groups separately with t-test and Pearson $\chi 2$ test. Parameters with significant data had logistic regression analysis performed. Later for all patients and then for intermediate-risk group patients, postoperative data were assessed in PNI positive and negative groups with t-test and Pearson $\chi 2$ test. Additionally all patients and intermediate-risk group patients were assessed with Kaplan–Maier survival analysis according to PNI distribution to research RFS in patients. For statistical analysis Statistical Package for the Social Sciences (SPSS, Version 20.0; SPSS, Chicago, III) was used and a p value $\leq$ 0.05 was accepted as significant.

Results

Among 380 patients with a mean follow-up duration of 34.5 months, PNI positivity rate on PNB pathology was identified as 22.9%. In other words, in 87 patients PNI was present, while PNI was absent in 293 patients. Of these 380 patients, 251 (66%) had T2 stage, while 129 (33.9%) had T3 stage on RRP pathology. Additionally while BR was observed in 76 (20%) patients, 304 (80%) patients were recurrence free. T2 and T3 groups were categorized as PNI positive and negative groups and BR positive or negative groups. PSA values, PNB pathology data of these groups and results are comparatively presented in Table 1. In the T3 group, PSA, PSA density, PNB GS, core number and tumor percentage, PNI positivity and D'Amico intermediate-risk and high-risk patient rates were observed to be significantly high

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