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Prostate Cancer

Risk Factors for Intraprostatic Incision into Malignant Glands at Radical Prostatectomy

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Abstract

Background: Histologically identified intraprostatic incision (IPI) into malignant glands is associated with an increase in biochemical recurrence following radical prostatectomy (RP). However, the predictor of IPI is poorly evaluated.

Objective: To evaluate the risk factors for IPI into cancer during RP for clinically localized prostate cancer (PCa).

Design, setting, and participants: Between January 1993 and July 2013, 19 986 men with clinically localized PCa underwent RP at our institution. This study includes 14 434 cases that had complete clinicopathologic data. IPI was defined as an iatrogenic incision into the prostate resulting in the presence of malignant glands at the inked surgical margin, regardless of accompanying pathologic features.

Intervention: Open, retropubic, robot-assisted laparoscopic and pure laparoscopic RP.

Outcome measurements and statistical analysis: Univariate and multivariable logistic regression analyses were conducted for risk factors of IPI in RP specimens.

Results and limitations: The overall incidence of IPI into malignant tissue was noted in 410 (2.8%) cases. In multivariable analysis, obesity, lower prostate weight, surgeon experience, and pure laparoscopic RP were associated with a higher risk of IPI. The odds ratios (OR) for body mass index and prostate weight were 1.05 (95% confidence interval [CI], 1.03–1.08; $p < 0.001$) and 0.99 (95% CI, 0.98–0.99, $p < 0.001$), respectively. The ORs for surgeon experience (>250 cases) and pure laparoscopic RP compared to open RP were 0.71 (95% CI, 0.55–0.90, $p = 0.005$) and 2.05 (95% CI, 1.35–3.11; $p = 0.001$), respectively.

Conclusions: The risk of IPI during RP is higher in men with obesity and lower prostate weight. In addition, a pure laparoscopic RP and the early series of each surgeon were associated with a higher risk of IPI. However, tumor characteristics were not associated with the IPI occurrence.

Patient summary: Intraprostatic incision occurrence is associated with obesity, small prostate, and surgeon experience and laparoscopic technique but not Gleason score and tumor stage.

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1. Introduction

Radical prostatectomy (RP) is a commonly performed procedure for treating clinically localized prostate cancer (PCa). Attempts have been made to evaluate the quality of RP through assessment of surgical margin status [1]. Positive surgical margin (PSM) is associated with decreased biochemical recurrence-free survival, as well as PCa specific survival [2]. However, PSM is significantly influenced by tumor characteristics such as Gleason score and pathologic stage. Therefore, it may not be the best quality tool for assessing the surgical technique.

PSM may occur as a consequence of intraprostatic incision (IPI), also known as capsular incision, when a surgeon inadvertently transects into an intraprostatic tumor [3–6]. Because histologic boundaries of the prostate are vague and benign prostate glands are seen admixed with skeletal muscle in the apex [5], a recent update recommended using IPI, not capsular incision, to describe this condition [4]. IPI has a significant negative impact on patient outcome following RP [6–9]. A high probability of IPI in obese patients could predict difficulty in achieving the optimal surgical approach and outcome, and it could also negatively impact disease-free survival of these men [10,11]. If the IPI rate is similar across the pathologic stage, IPI may be potentially used as a marker of violation of the surgical plane independent of tumor characteristics, and a tool to assess surgical quality. In addition, it is unclear what perioperative factors influence IPI.

In this study, we examined the prevalence of IPI according to pathologic stage using a large cohort of patients who underwent RP in a single center with standardized pathologic examination of surgical specimens. Then we investigated the independent preoperative predictors of an IPI.

2. Patients and methods

Between January 1993 and July 2013, 19 986 men with clinically localized PCa underwent RP at our institution. This study included 14 434 men who had complete clinicopathologic data and those who received no neoadjuvant hormonal therapy. Cases with IPI into tumor were identified from RP final pathology reports. Our previous study on the impact of IPI on survival included only men with organ-confined

disease, excluding those with extraprostatic extension (EPE), seminal vesicle invasion, and/or lymph node metastasis [8]. However, in this current study, all men were included regardless of accompanying pathologic features.

RP specimens were sectioned as previously described [5]. IPI was defined as an iatrogenic incision into the prostate resulting in the presence of malignant glands at the inked surgical margin. Cases with tumor extending to the inked margins in the same plane where benign prostatic glands also extended to those margins were considered to have a PSM due to IPI. At the apex, if the tumor was unassociated with benign prostatic glands at the inked edge, the tumor was classified as having a positive margin in an area where it was unclear if there was a PSM associated with EPE or IPI due to ambiguities of where the edge of the prostate was in this region; these cases were not considered in the current study as having IPI. Equivocal cases of whether or not IPI was present were reviewed and reclassified [5]. Prostate weight was determined by measuring gross RP specimen weight, including the seminal vesicles and vasal tips before October 2010, and excluding those after this date.

Differences in age, preoperative prostate-specific antigen (PSA), body mass index (BMI), prostate weight, surgery year, race, clinical stage, biopsy Gleason sum, operation type (open radical retropubic prostatectomy, pure laparoscopic RP, or robot-assisted laparoscopic RP [RARP]), and surgeon experience according to presence of IPI were compared using the student *t* test for continuous variables and the chi-square test for categorical variables. Age at RP, preoperative PSA level, BMI, prostate weight, and surgery year were examined as continuous variables. Race (Caucasian, African American, and others), clinical stage (T1, T2, and T3), biopsy Gleason sum (≤ 6 , 7, ≥ 8), operation type, and surgeon experience were examined as categorical variables. To consider surgeon experience, an expert was defined as a surgeon who performed >250 cases in each operation type [12–14]. Univariate and multivariable logistic regression analyses were conducted to assess the prognostic significance of preoperative variables. All tests were two-sided, with $p < 0.05$ considered statistically significant. STATA 11.0 (Stata Corp., College Station, TX, USA) was used for the statistical analyses.

3. Results

Overall, IPI into malignant glands was diagnosed in 410 of the 14 434 RP specimens (2.8%). IPI was found in 289 (2.9%) for pT2, 97 (2.8%) for pT3a, 15 (3.0%) for pT3b, and 9 (3.1%) for pN+ ($p = 0.975$). Figure 1 shows that the probability of IPI was not associated with pathologic stages. However, the probability of PSM increased with advancing pathologic stage ($p < 0.001$). The probabilities of PSM in pT2, pT3a, pT3b, and pN+ were 4.2%, 30.6%, 30.1%, and 36.9%,

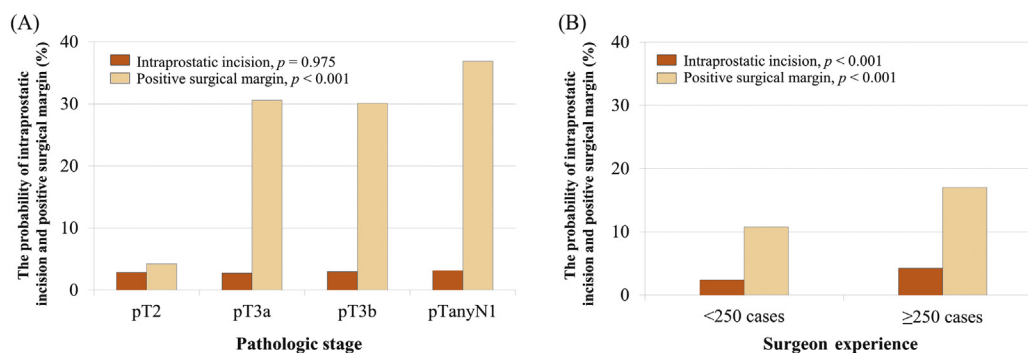


Fig. 1 – The probabilities of intraprostatic incision and positive surgical margin according to (A) pathologic stage and (B) surgeon experience. *P* values were calculated by chi-square test.

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