Discrepancy Between Local and Central Pathological Review of Radical Prostatectomy Specimens

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Abbreviations and Acronyms

CR = central review CRPC = Clinicopathological Research Group for Localized Prostate Cancer ECE = extracapsular extension GS = Gleason score ISUP = International Society of Urological Pathology LNI = lymph node involvement LR = local review PSA = prostate specific antigen PSM = positive surgical margin RP = radical prostatectomy SVI = seminal vesicle invasion

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Purpose: Pathological assessment of radical prostatectomy specimens has not been uniform among pathologists. We investigated interobserver variability of radical prostatectomy specimen reviews between local and central pathologists. **Materials and Methods:** We collated data from 50 institutions on 2,015 patients with cT1c-3 prostate cancer who underwent radical prostatectomy between 1997 and 2005. All radical prostatectomy specimens were retrospectively reevaluated by a central uropathologist. Gleason score, extracapsular extension, seminal vesicle invasion, lymph node involvement, positive surgical margin, year of diagnosis and pathology volume were recorded.

Results: The exact concordance rate of Gleason score between local and central review was 54.8%, and under grading and over grading rates at local review were 25.9% and 19.2%, respectively. Spearman's rank correlation coefficient was 0.61 for local and central radical prostatectomy Gleason score. The exact concordance rate of Gleason score 8-10 at local review was significantly lower than that of Gleason score 5-6, 3 + 4 and 4 + 3 at local review (p = 0.011, <0.001 and 0.006). Exact concordance rates between local and central review for extracapsular extension, seminal vesicle invasion, lymph node involvement and positive surgical margin were 82.5%, 97.6%, 99.6% and 87.5%, respectively. High volume institutions and recently diagnosed cohorts showed significantly higher exact concordance rates between local and central review for radical prostatectomy Gleason score and other pathological features (all p < 0.001).

Conclusions: High volume institutions and recent series show higher concordance between local and central review of radical prostatectomy pathology. However, concordance for high grade Gleason score, extracapsular extension and surgical margin status remains poor. Radical prostatectomy specimens should be reevaluated in a multi-institutional study for more accurate pathological data.

Key Words: pathology, prostatic neoplasms, prostatectomy

PATHOLOGICAL features of radical prostatectomy specimens such as Gleason score, extracapsular extension, seminal vesicle invasion, lymph node involvement and positive surgical margin are crucial observations for physicians to assess the prognosis of each patient. Various nomograms predicting PSA relapse after RP have been constructed based on these pathological features combined with preoperative PSA.^{1–3} Therefore, ideally these features should be diagnosed uniformly among pathologists. However, there is concern about interobserver variability for pathological features of RP specimens, which would affect prognostic accuracy.

Interobserver variability for biopsy GS among pathologists is well documented.^{4–9} Biopsy GS assigned by pathologists at an academic center has been reported as better correlated with RP GS than that by pathologists at community centers.^{4,9} However, to our knowledge interobserver variability for RP GS has not been investigated in a large contemporary RP series.

There are only a few studies of interobserver variability for other pathological features of RP specimens.^{10–12} It was reported that the exact concordance between local and central review of RP specimens for ECE, SVI and PSM was 57.5%, 94.0% and 69.4%, respectively, in patients with pT3/PSM.¹¹ On the other hand, expert uropathologists indicated good concordance when evaluating ECE (91.2%, $\kappa = 0.63$) and PSM (90.4%, $\kappa = 0.74$).¹²

We investigated the interobserver variability between local and central pathologists for RP pathological features in a large RP series of 2,015 patients. Central review for GS was based on the 2005 ISUP consensus. In addition, we analyzed the impact of the date of diagnosis and pathology volume on interobserver variability.

MATERIALS AND METHODS

Patient Population

The CRPC disease registry collates data on clinically localized prostate cancer accrued from 108 academic and community practices throughout Japan. Between 1997 and 2005 patients with clinically localized (cT1c-3) prostate cancer who underwent RP were enrolled in the CRPC registry after obtaining institutional review board approval from each center.

Of these CRPC patients pathological slides of biopsy and prostatectomy specimens were available from 50 institutions in 2,015 patients with no preoperative therapy. In all patients preoperative diagnosis was made by systemic biopsy (6 or more cores). Preoperative serum PSA was known for all patients. Clinical stage was determined by digital rectal examination and was assigned according to the 2002 American Joint Committee on Cancer staging system.

Pathological Assessment

Prostatectomy specimens from the patients were processed by a whole mount technique after formalin fixation at each institution.¹³ All pathological slides of biopsy specimens were reviewed by a uropathologist (TS). All pathological slides of RP specimens were reviewed by 1 uropathologist (KK) who has reviewed more than 5,000 RP cases. GS was assigned according to the 2005 ISUP consensus, and categorized into 5 groups of 2–4, 5–6, 3 + 4, 4 + 3 and 8–10.¹⁴ Global GS that considered the entire tumor within the prostate as 1 lesion was recorded for RP specimens since the GS of each tumor was not available in the original reports for most patients. The exact concordance rate for categorized Gleason score between original (local) and central review was investigated. Tertiary Gleason pattern in RP specimens was not reflected as primary or secondary pattern on the final RP GS.

The presence of ECE, SVI, LNI and PSM was recorded for all RP specimens. ECE level was further categorized as focal ECE and established ECE.¹⁵ ECE was assigned as positive when tumor cells existed beyond the confines of the prostate.¹⁶ Direct contact between tumor cells and adipose tissue was not needed to assign ECE. The presence of tumor cells at the inked margin of resection was considered a PSM. For specimens that had not been inked before formalin fixation the presence of tumor cells at the noninked margin of resection was considered a PSM. SVI was assigned as positive when tumor cells had invaded into the muscular coat of the extraprostatic seminal vesicle. The positive to negative rate for ECE, SVI, LNI and PSM was defined as No. centrally negative cases in locally positive cases/No. locally positive cases. The negative to positive rate was defined conversely.

Data from original pathological reports for RP GS, ECE, SVI, LNI and PSM were available in 1,774, 1,630, 1,639, 1,914 and 1,579 patients, respectively. All data for ECE, SVI, LNI and PSM were available in 1,526 patients. For influence of date of diagnosis we compared patients diagnosed by local pathologists in 1997 to 2003 with those diagnosed in 2004 to 2005. For pathology volume we defined high volume institutions as those contributing 100 or more patients to the CRPC registry and low volume institutions as those contributing less than 100 patients.

Statistical Analysis

Spearman's rank correlation coefficient (r) on the relationship of RP GS was generated. Simple kappa statistics were used for concordance between local and central review in ECE, SVI, PNI and PSM. The chi-square test was used for comparison of the exact concordance rate between local and central review for each pathological feature. All p values are 2-sided and p < 0.05 considered significant.

RESULTS

Preoperative Characteristics

Median patient age was 66 years (range 42 to 84) and median PSA was 8.5 ng/ml (range 0.5 to 85.9). A total of 1,327 patients (65.9%) had cT1c disease. For biopsy specimens the distribution of central biopsy GS 2–4, 5–6, 3 + 4, 4 + 3 and 8–10 was 0.1% (2), 33.6% (677), 27.4% (552), 19.0% (382) and 20.0% (402), respectively (table 1).

Concordance for RP GS

Table 2 shows concordance for RP GS between local and central review. Spearman's rank correlation coefficient was 0.61 for local and central RP GS. Overall exact concordance between central and local review was 54.8%, and the under grading and over grading rate in local review was 25.9% and 19.2%, respectively. When GS 3 + 4 and 4 + 3 were combined the exact concordance rate was 66.0%. All 67 cases with local review GS 2–4 were upgraded to GS Download English Version:

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