Prostate gland biopsies and prostatectomies: an Ontario community hospital experience

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Abstract

Objective: Transrectal ultrasound–guided core biopsies of the prostate gland and prostatectomies have become common procedures at many community hospitals in Canada, especially in the era of serum prostate-specific antigen (PSA) screening for prostate cancer. The Gleason grading of prostate cancer in biopsies and prostatectomies is a major determinant used for treatment planning. There is evidence in the literature that suggests important discordance between community hospital pathologists and urological pathologists with respect to the Gleason grading of prostate cancer. Our objective was to determine the diagnostic rates and Gleason scoring patterns for prostate gland biopsies and prostatectomies at our institution compared with the literature.

Methods: We conducted a retrospective review of all prostate gland biopsies and prostatectomies performed at the Grey Bruce Health Services from January 2005 to September 2005. We collected data from 194 biopsies and 44 prostatectomies. We obtained prebiopsy serum PSA levels and digital rectal exam results for all patients from urologists' office records.

Results: The average age for men having biopsies was 65.8 (standard deviation [SD] 8.6) years, and the average prebiopsy serum PSA level was 8.7 (median 7.1, SD 6.2) µg/L. The rates of diagnosis from prostate gland biopsies of benign (17.6%), high-grade prostatic intraepithelial neoplasia (11.0%), atypical small acinar proliferation suspicious for invasive malignancy (13.2%) and invasive prostatic adenocarcinoma (58.2%) at our institution were significantly different than those reported in the literature ($p < 0.001$). We observed a significant variation in the rates of these diagnoses among the community hospital pathologists in our study ($p = 0.004$). There was a strong correlation between the increasing number of positive core biopsy sites and increasing Gleason scores in biopsies ($p < 0.001$). There was also a strong correlation between increasing prebiopsy serum PSA levels and increasing Gleason scores in biopsies ($p < 0.001$). A substantial proportion (21.9%) of the biopsies given the Gleason score of 6 had a Gleason score of 7 in the prostatectomy specimen.

Conclusion: Our results showed a significant difference in prostate gland biopsy categorical diagnoses compared with the literature. There were also significant differences in categorical diagnoses of prostate gland biopsies among the community hospital pathologists in our study. The data identify a strong positive correlation between the increasing number of positive core biopsy sites and increasing Gleason scores in biopsies, as well as a strong positive correlation between increasing prebiopsy serum PSA levels and increasing Gleason scores in biopsies that revealed cancer. We would encourage other community hospital pathologists, in collaboration with their urologists, to review periodically their prostate gland pathology practices in an attempt to improve the uniformity of diagnoses.

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Introduction

Transrectal ultrasound–guided core biopsies of the prostate gland and prostatectomies have become common procedures at many community hospitals in Canada, especially in the era of serum prostate-specific antigen (PSA) screening for prostate cancer. The Gleason score[1] is a required element in pathology reports that assists urologists and oncologists to decide what treatments they should recommend to patients with invasive prostatic adenocarcinoma. A poor correlation between general pathologists and urological pathologists with respect to Gleason grading has been reported.[2–8] Community hospital pathologists have been reported to "undergrade" prostate cancer in biopsy material. It has been suggested that all cancers that community hospital pathologists diagnose based on prostate gland biopsies should be reviewed by a urological pathologist before definitive treatment.[9]

Our objective was to compare the reporting of prostate gland biopsies and prostatectomies in our community hospital with data in the literature and to assess the homogeneity of prostate gland pathology reporting among the pathologists at our institution.

Methods

The Grey Bruce Health Services is a 240-bed community hospital in rural Ontario

with a catchment population of 157 000. There are 3 urologists and 3 pathologists at our institution. All 6 are active participants in the prostate pathology service.

We searched the pathology database at the Grey Bruce Health Services retrospectively from Jan.1, 2005, to Sept. 31, 2005. We retrieved pathology reports for all prostate gland biopsies and prostatectomies for this 9-month period. We also retrieved prostate gland biopsy reports for patients who had a prostatectomy with biopsy before Jan. 1, 2005. The Grey Bruce Health Services Ethics Committee approved our study.

The urologists at our institution perform transrectal ultrasound–guided core biopsies, obtaining 2 cores from each site (left base, left mid, left apex, right base, right mid and right apex). They submit the biopsies from each site in separate specimen containers in 10% formalin. More than 95% of the biopsies submitted contain 12 cores of tissue. We report prostate gland biopsies and prostatectomies using a synoptic-like report adapted from templates developed by the College of American Pathologists. Our reports meet the criteria established by Cancer Care Ontario for the reporting of prostate gland biopsies and prostatectomies.

We collected the following data from each biopsy report: age, the most severe diagnostic abnormality in each set of biopsies (benign, high-grade prostatic intraepithelial neoplasia (HGPIN), atypical small acinar proliferation (ASAP) suspicious for cancer, invasive prostatic adenocarcinoma, urologist (R.D., P.M., T.W.), and pathologist (K.N., B.R., B.S.). For patients who received a diagnosis of invasive adenocarcinoma at biopsy and for all prostatectomies, we collected the following additional data: Gleason score; number of biopsy sites positive for cancer; and the presence or absence of perineural invasion, angiolymphatic invasion and extraprostatic extension. We obtained the prebiopsy serum PSA level and the findings of the digital rectal exam immediately before biopsy from the urologists' office records. Data were available for all patients who had a biopsy and a prostatectomy.

We compiled all of the data in an Excel (Microsoft Corp.) spreadsheet and performed statistical analyses using SAS9 software (SAS Inc.).

Results

We performed 194 sets of prostate gland biopsies on 182 patients during the study period. Ten patients had 2 sets of biopsies and 1 patient had 3 sets. For the patients who had repeat biopsies, 8 had received a previous diagnosis of HGPIN and 3 had a previous diagnosis of ASAP. We included in our analysis only the first set of prostate gland biopsies for each patient. The mean age of the patients who had biopsies was 65.8 (standard deviation [SD] 8.6, range 41–89) years and the mean prebiopsy serum PSA level was 8.7 (SD 6.2, median 7.1, range 0.3–47.5) μg/L, excluding 1 outlier value of 107 μg/L. Table 1 shows that for each pathologist there was no significant difference in patient age (F test, p = 0.39) or prebiopsy serum PSA (Kruskal–Wallis [Mann–Whitney-Wilcoxon] test, p = 0.24) among the pathologists. The majority of patients (108, 59.3%) had prebiopsy serum PSA levels between 4.0 and 10.0 μg/L. About one-quarter of patients (52, 28.6%), had prebiopsy serum PSA levels greater than 10.0 μg/L. A minority of patients (22, 12.1%) had serum PSA levels lower than 4.0 μg/L; results of the digital rectal examinations of all of these patients were abnormal.

Table 1. Characteristics of patients who had biopsies and prostatectomies, by participating study pathologist

Pathologist	No. of patients	Mean (SD) age, yr	Mean (SD) prostate-specific antigen level, μg/L
A	65	66.8 (8.9)	9.0 (6.6)
B	65	66.1 (8.1)	9.2 (6.7)
C	52	64.4 (8.6)	7.6 (4.9)
All biopsies	182	65.8 (8.6)	8.7 (6.2)
All prostatectomies	44	62.7 (5.8)	7.9 (4.1)

SD = standard deviation.

Table 2 shows the distribution of diagnoses for each pathologist and the total distribution for our institution compared with rates published in the literature. The rate of diagnosis of invasive prostatic adenocarcinoma at our institution (58.2%) was 1.8 times greater than that reported in the literature (33%). Our rate of precancer diagnoses (HGPIN and ASAP, 24.2%), was 2.0 times greater than that reported in the literature. The rate of benign diagnoses (17.6%) was 3.1 times lower than that reported in the literature. The rates of all diagnoses at our institution were significantly different than those reported in the literature (χ^2 test, $p < 0.001$).

We observed significant variation among pathologists at our institution with respect to the rendering of categorical diagnoses in prostate gland biopsies (χ^2 test, $p = 0.004$) (Table 2). The majority of cancers (84.9%) were given a Gleason score of 7 (49.1%) or 6 (35.8%). There were no cancers given a Gleason score of less than 6 at biopsy. There was significant variation among the pathologists with respect to the Gleason grading of cancers diagnosed at biopsy (χ^2 test, $p = 0.001$) (Table 3). There was a strong correlation in the biopsies between the increasing number of positive core biopsy sites and increasing Gleason scores (Spearman correlation test, $p < 0.001$) (Table 4). There was also a strong correlation in the cancerous biopsies between increasing prebiopsy serum PSA levels and increasing Gleason scores (Spearman correlation test, $p < 0.001$) (Table 5).

Table 2. Categorical diagnoses (*n* = 182) and distribution at biopsy, by participating study pathologist

	Diagnostic category; no. (%) of patients			
Pathologist	Benign	HGPIN	ASAP	Cancer
A	19	4	7	35
B	5	11	14	35
C	8	5	3	36
Totals	32 (17.6)	20 (11.0)	24 (13.2)	106 (58.2)
Literature	(55.0)	(7.0)	(5.0)	(33.0)

ASAP = atypical small acinar proliferation; HGPIN = high-grade prostatic intraepithelial neoplasia.

Table 3. Gleason score distribution for cancers diagnosed at biopsy (*n* = 106), by participating study pathologist

	Gleason score; no. (%) of patients		
Pathologist	6	7	8/9
A	13	17	5
B	4	22	9
C	21	13	2
Totals	38 (35.8)	52 (49.1)	16 (15.1)
Literature	(49.0)	(41.0)	(10.0)

Table 4. Number of positive core biopsy sites per case versus Gleason score for cancers diagnosed at biopsy (*n* = 106)

	No. of positive core biopsy sites per patient					
Gleason score	1	2	3	4	5	6
6	17	11	5	3	2	0
7	6	13	15	9	2	7
8/9	2	2	7	4	0	1
Totals	25	26	27	16	4	8

We performed immunohistochemistry for the presence of basal cells (cytokeratin 34βE12) on 74/182 biopsies (40.7%). We sent a minority of biopsies (16, 8.8%) for external consultation to the group of urological pathologists at the London Health Science Centre in London, Ont. We forwarded the majority (14 /16) with a diagnosis of "atypical small acinar proliferation suspicious for invasive malignancy" to determine whether there were sufficient features for a definitive diagnosis of invasive prostatic adenocarcinoma. We forwarded the remaining 2 for confirmation of Gleason grading. The consultant urological pathologists diagnosed "minimal" cancer in 8/14 (57%) of the cases in which we suspected cancer.

The comparison of prostate gland biopsies and prostatectomies showed that there was a marked increase in the reporting of perineural invasion in the prostatectomy specimens (Table 6). We never reported angiolymphatic invasion and extraprostatic extension in the biopsy specimens, yet 7/44 (15.9%) tumours showed extraprostatic extension at prostatectomy. We reported seminal vesicle invasion in 3/44 (6.8%) prostatectomies. There were 36 pT2 tumours and 8 pT3 tumours in our study. A large proportion of cancers diagnosed at biopsy and given a Gleason score of 6 (38.9%) received a final Gleason score of 7 at prostatectomy. We sampled lymph nodes in 38/44 (86.3%) prostatectomies. All of the lymph nodes sampled were free of cancer. Surgical margins were positive for cancer in 15/44 (34.1%) prostatectomy specimens.

Discussion

The rate of diagnosis of invasive prostatic adenocarcinoma at our institution (58.2%) was substantially higher than the average rate (33%) reported in the literature.[10,11] We compared the rates of categorical diagnoses in our study with those reported in 2 large-scale studies involving 78 290 patients.[10,11] Although our population may not have been directly comparable to these large-scale predominantly American studies, in the absence of similar large-scale Canadian data, we used the rates of categorical diagnoses in these studies for comparison. The demographics and prebiopsy serum PSA levels of our patient population compare favourably with those reported in the literature.[11] Our results raise the possibility that there are important differences between the

Table 5. Correlation between diagnostic category and prebiopsy prostate specific antigen level

Diagnosis	No. of patients	Mean (SD) prostate-specific antigen level, µg/L
Benign	32	8.9 (7.2)
HGPIN	20	6.4 (3.6)
ASAP	24	7.1 (4.2)
All cancers	106	9.4 (6.6)
Gleason score		
6	38	6.8 (3.2)
7	52	9.9 (7.4)
8/9	16	13.9 (7.3)

ASAP = atypical small acinar proliferation; HGPIN = high-grade prostatic intraepithelial neoplasia; SD = standard deviation.

Table 6. Characteristics of cancers diagnosed at biopsy v. at prostatectomy (*n* = 44)

	Gleason score			Pathologic feature		
Procedure	6	7	8/9	PN	AL	EPE
Biopsies	18	24	2	13	0	0
Prostatectomies	11	32	1	38	1	7

PN = perineural invasion; AL = angiolymphatic invasion; EPE = extra-prostatic extension.

approaches to prostate gland biopsies performed by American and Canadian urologists. We speculate that Canadian urologists, who work in a single-payer environment with limited resources, may have more stringent criteria for deciding to what patients they will offer a prostate gland biopsy. Alternatively, the widespread use of serum PSA screening for prostate cancer may have been delayed in our geographic region. This would suggest that the increased rate of prostate cancer that we observed in the biopsies may be secondary to case-finding in the initial wave of more widespread serum PSA screening. Regardless of the definitive explanation for our findings, we question whether Canadian urologists should be performing greater numbers of prostate gland biopsies.

Our results showed an increased rate of precancer diagnoses (HGPIN and ASAP, 24.2%) compared with the rate reported in the literature (13%).[10–13] The literature indicates that these precancer diagnoses show poor interobserver reproducibility among community hospital and urological pathologists.[12–15] Several recent reviews outlined the diagnostic criteria and the clinical significance of HGPIN and ASAP in prostate gland biopsies.[12–15] It is possible that the more widespread publication of diagnostic criteria for these precancer diagnoses will lead to greater degrees of diagnostic homogeneity among community hospital pathologists. Regardless, the increased rates of precancer diagnoses at our institution are an important and possibly worrisome trend, in that HGPIN and ASAP have been indications for early repeat biopsies by the urologists at our institution. We would again speculate that the increased rates of precancer diagnoses may be related to a selection bias as described above.

The data show that there are significant differences among the pathologists at our institution in the Gleason grading of prostate cancers at biopsy. Significant variation in the grading of prostate cancer has been reported previously among general and urological pathologists.[2–7,16] Without review of all of these prostate gland biopsies by an expert urological pathologist, it would not be possible to determine if an individual pathologist was "under-" or "overgrading." Previous studies have indicated that community pathologists have a tendency to undergrade prostate cancer biopsies compared with urological pathologists.[2,4–6,8] There was no evidence of this phenomenon at our institution. Recent studies have shown that a teaching program by an expert urological pathologist and/or the completion of a Web-based tutorial can substantially improve the grading of prostate cancer by community hospital pathologists.[6,8,17] The results of our study suggest that such a program may be beneficial in our department to improve the homogeneity of Gleason grading in biopsy specimens. Alternatively, a formal inter- and intraobserver variability study at our institution may be beneficial.

We observed significant positive correlations between the increasing number of positive core biopsy sites and Gleason scores in biopsies, as well as between increasing prebiopsy serum PSA levels and increasing Gleason scores in biopsies. These data agree well with previous studies that have associated increasing cancer volume with increasing Gleason score.[18] The data also agree with studies suggesting that prebiopsy serum PSA levels are predictive of biopsy Gleason scores.[19] The results from our study also show that the prebiopsy serum PSA levels are useful markers for the stratification of risk in patients in whom cancer was diagnosed at biopsy.

A large proportion (38.9%) of cancers diagnosed at biopsy and given a Gleason score of 6 were given a final Gleason score of 7 at prostatectomy.[2,20,21] This upgrading of prostate cancers and its clinical importance has been reported recently in a study by urologists and urological pathologists at the University Health Network in Toronto.[21] Our experience agrees well with that reported in previous studies. It has been suggested that the upgrading of prostate cancers at prostatectomy is most likely related to sampling error at the time of biopsy.[2] The increase in non–organ confined cancers (pT3 tumours) at prostatectomy compared with biopsy is also most likely related to a sampling error at the time of biopsy. The data from our study indicate that the observed increase in Gleason score at prostatectomy is not substantially different than that observed at a nearby tertiary care centre.

Conclusion

The rates of cancerous, precancerous (HGPIN and ASAP) and benign diagnoses in prostate gland biopsies at our institution were significantly different

than those reported in the literature. There was also significant variation in the rates of categorical diagnoses and Gleason grading in biopsies among the community pathologists in our study. Based on the results presented, we would encourage other community hospital pathologists, in collaboration with their urologists, to review periodically their prostate gland pathology practices in an attempt to improve the uniformity of diagnoses and Gleason grading. Since this is the first Canadian publication to report rates of diagnoses from a community hospital, we hope that the data can serve as a reference for other Canadian community hospital pathologists who undertake a similar review.

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