Prostate Carcinoma Presentation, Diagnosis, and Staging

An Update from the National Cancer Data Base

David C. Miller, M.D.[1]
Khaled S. Hafez, M.D.[1]
Andrew Stewart, M.A.[2]
James E. Montie, M.D.[1]
John T. Wei, M.D.[1]

[1] Department of Urology, University of Michigan, Ann Arbor, Michigan.

[2] Commission on Cancer, American College of Surgeons, Chicago, Illinois.

BACKGROUND. Based on the 1998 Patient Care Evaluation (PCE) from the American College of Surgeons National Cancer Data Base (NCDB), the authors described contemporary nationwide patterns of prostate carcinoma presentation, diagnosis, and staging.

METHODS. The authors reviewed 54,212 cases from the 1998 PCE. Demographics, presenting signs and symptoms, tumor characteristics, prostate biopsy techniques, and use of staging modalities were evaluated.

RESULTS. The mean age of patients in the sample was 68 years. Among patients with available data, 87.5% had a prostate specific antigen (PSA) level of 4 ng/mL or higher, 83.1% had American Joint Committee on Cancer (AJCC) Stage I–II lesions, 80.2% had well or moderately differentiated cancers, and 68.7% of newly diagnosed patients were asymptomatic. Compared with symptomatic patients, asymptomatic patients were more likely to have localized disease (84.6% vs. 78.2%, $P < 0.01$) and well or moderately differentiated tumors (82.2% vs. 74.6%, $P < 0.01$). Transrectal ultrasound- guided prostate biopsy was the most common method of tissue confirmation (45.4%). Radionuclide bone scintigraphy was the most frequently employed staging modality (48.7%). Use of various staging evaluations was more frequent among patients at increased risk for disseminated disease (PSA $>$ 10 ng/mL and/or high-grade tumors) versus patients at lower risk (PSA $\leq$ 10 and low to moderate-grade tumors) for metastatic disease ($P < 0.005$).

CONCLUSIONS. Most newly diagnosed patients with prostate carcinoma are asymptomatic and have moderately differentiated and organ-confined disease. Compared with symptomatic patients, tumors in asymptomatic men are associated with lower pretreatment PSA levels, AJCC stage, and tumor grade. Selective use of staging evaluations, based on risk of metastatic disease, may be relatively uncommon. The NCDB remains a unique and rich source of novel patient care information and serves as a national point of reference for prostate carcinoma presentation, diagnosis, and staging. ***Cancer* 2003;98:1169–78.**

KEYWORDS: prostate carcinoma, screening, diagnosis, staging.

The American College of Surgeons Commission on Cancer (CoC) National Cancer Data Base (NCDB) was established to evaluate nationwide patterns of cancer presentation, care, and outcomes. Earlier reports from the NCDB have provided a wealth of information regarding prostate carcinoma diagnosis, staging, and therapy through the middle of the last decade.[1–6] The prostate specific antigen (PSA) era has been marked by a considerable shift in the number of incident cases of prostate carcinoma, as well as a stage migration toward a higher proportion of localized tumors.[2,7] Moreover, the advent of PSA

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Address for reprints: John T. Wei, M.D., Department of Urology, Taubman Health Care Center, University of Michigan Health System, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0330; Fax: (734) 936-9127; E-mail: jtwei@umich.edu

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testing prompted the development of various guidelines for optimal screening of asymptomatic men and staging of patients with newly diagnosed cancers.[2,8] The current study reviews the findings from the 1998 NCDB prostate carcinoma Patient Care Evaluation (PCE) and describes contemporary nationwide patterns of presentation, diagnosis, and staging of adenocarcinoma of the prostate. Unique to this report from the NCDB is the availability of pretreatment PSA levels and information on patient symptoms at the time of presentation, particularly among African-Americans and patients with a positive family history. Also included in the current review is an evaluation of prostate carcinoma staging practices in patients at variable risk for metastatic disease.

MATERIALS AND METHODS

The NCDB is a joint endeavor of the CoC of the American College of Surgeons and the American Cancer Society (ACS). Data from the NCDB have been compared in a previous study with the population-based Surveillance, Epidemiology and End Results (SEER) registry and shown to be similar in terms of patient and disease characteristics.[9] NCDB data are collected using a standardized, electronic data abstraction format that has been described previously.[5–7]

Sample and Population

In 1998, 1504 hospitals submitted data to the NCDB. Of these, 66% (990 hospitals) participated in the prostate carcinoma PCE. Individual hospital registries were requested to provide demographic and clinicopathologic information on cases with histologically proven prostate carcinoma that was diagnosed and/or initially treated at their institution between January 1, 1998 and December 31, 1998. Therefore, these cases represent a prospective convenience sample rather than a statistical sample from a defined population. Initially, 64,909 cases were entered into the study. Of these, 7005 cases were ineligible because the date of diagnosis was outside the stated study parameters or because treatment was initiated at a facility other than the reporting institution. An additional 1947 cases were determined to be clinical duplicates or eligible cases that were reported by more than one registry. When this occurred, it is the protocol of the NCDB to retain the case with more comprehensive clinical information and to exclude the other(s). Of the remaining 55,957 cases, only those with an ICD-0-2 primary site of C61.9 (prostate gland), histology code of 8140, and behavior codes of 2 or 3 (adenocarcinoma in situ and adenocarcinoma, not otherwise specified [NOS], respectively) were retained for analysis, providing a final study population of 54,212 cases.[10] The number of cases retained for analysis per participating hospital ranged from 1 to 387, with the mean number of cases per hospital equal to 55.

Variables and Procedures

When available, several baseline demographic and clinical parameters were determined for each patient including age, race, pretreatment serum PSA (ng/mL), stage, and grade. Ethnic/racial categories in the registry data include white, black, American Indian, Chinese, Japanese, Filipino, Hawaiian, Puerto Rican, Hispanic, and other/unknown. For the current study, white race includes Caucasians of non-Spanish origin, whereas African-American comprises all patients reported as black.

The study utilized the American Joint Committee on Cancer (AJCC) staging system.[2,11] The AJCC stage data represents a "best" staging system whereby the reported stage is the pathologic stage whenever this was available and clinical stage (about 56% of cases) when the former was unavailable. Therefore, pathologic stage, when available, is provided to the exclusion of clinical stage. This system is consistent with previous NCDB reports.[2,7]

Descriptions of histologic grade have been described in previous reports from the NCDB.[2,7] Differentiation between biopsy and prostatectomy tumor grade was not captured as part of the study design.

The study design explicitly requested documentation of the presence or absence of specific, relevant symptoms (low back pain, hematuria, and/or difficulty with urination) at the time of initial diagnosis. This allowed classification of cases as asymptomatic (i.e., detected by abnormal PSA and/or digital rectal examination [DRE]) or symptomatic (regardless of PSA and/or DRE findings). Various techniques for tissue confirmation of prostate carcinoma (e.g., transrectal ultrasound-guided biopsy [TRUS], needle biopsy NOS, perineal biopsy, transurethral resection [TURP], digital biopsy, and cytology) were abstracted explicitly from the medical record. The utilization of prostate carcinoma staging modalities is also characterized, including radionuclide bone scans, computed tomography (CT) scans of the abdomen and/or pelvis, magnetic resonance imaging (MRI) scans, and pelvic lymph node dissection. For each staging modality, we determined the proportion of patients with results suggestive for tumor dissemination. In addition, patients were stratified, using pretreatment PSA and tumor grade, into high-risk (PSA level $>$ 10 ng/mL and/or poorly differentiated [Grades 3 and 4] cancers), and low-risk (PSA $\leq$ 10 ng/mL and well or moderately differentiated [Grades 1 and 2] cancers) groups based on their likelihood of having extraprostatic disease at

TABLE 1
Demographic Characteristics of Men Entered into the 1998 Patient Care Evaluation Study

Characteristics	No. of subjects	% of subjects
Patient age (yrs)	*n* = 54,188 (99.9%)[a]	
Mean age (SD)	67.99 (8.82)	
< 50	1046	1.9
50–59	8364	15.4
60–69	20,489	37.8
70–79	19,739	36.4
≥ 80	4550	8.4
Race	*n* = 53,340 (98.4%)[a]	
White	43,675	80.9
Black	6736	12.6
Other race	2929	5.5
Family history of prostate carcinoma	*n* = 38,341 (70.7%)[a]	
None	32,430	84.6
Affected, first-degree relative	5173	13.5
Affected, non–first-degree relative	536	1.4
Affected, unknown relationship	202	0.5

SD: standard deviation.
[a] Total number of cases in the 1998 Patient Care Evaluation is 54,212. Discrepancy represents missing or unknown data points.

TABLE 2
Pretreatment Prostate Specific Antigen, American Joint Committee on Cancer Stage (1997 Classification), and Tumor Grade

Characteristics	No. of subjects	% of subjects
Pretreatment PSA (ng/mL)	*n* = 33,179 (61.2%)[a]	
< 4	4145	12.5
4–10	17,537	52.9
10.1–20	6225	18.8
> 20	5272	15.9
AJCC stage	*n* = 51,459 (94.9%)[b]	
1	3102	6.0
2	39,674	77.1
3	5395	10.5
4	3288	6.4
Tumor grade	*n* = 51,322 (94.7%)[b]	
1 (well differentiated)	4763	9.3
2 (moderately differentiated)	36,382	70.9
3 (poorly differentiated)	9978	19.4
4 (undifferentiated)	199	0.4

PSA: prostate specific antigen; AJCC: American Joint Committee on Cancer.
[a] The results from two of the commercial registry software vendors that support the National Cancer Data Base were excluded for technical reasons. As a result, specific pretreatment prostate specific antigen values are reported for only 33,179 cases.
[b] Total number of cases is 54,212. Discrepancy represents missing or unknown data points.

the time of diagnosis. This risk stratification allowed analysis of staging evaluations in the context of recently published practice guidelines.[12,13]

Descriptive statistics were used to evaluate the frequencies, percentages, measures of central tendencies, and variation. Given the large number of cases included in these analyses, statistically significant differences might result even in comparisons with clinically insignificant differences. Therefore, formal tests of comparisons were limited to specific situations for which we had a priori hypotheses. For these analyses, differences in proportion were evaluated using the chi-square test at a significance level of 5%. Statistical analyses were conducted using SPSS version 10 software (SPSS, San Diego, CA).

RESULTS

Patient Characteristics

Demographic data for patents included in the 1998 PCE are provided in Table 1. The mean age for men included in the 1998 analysis was 68.0 ± 8.8 years. In this cohort of patients, 32.9% of patients were younger than 65 years of age, 1.9% of patients were younger than 50 years of age, 8.4% were older than 80 years of age, 12.6% of patients were African-American, and 15.4% had a family history of prostate carcinoma.

Tumor Characteristics

Pretreatment PSA levels were available for 61.2% of cases and are summarized in Table 2. Among patients with available data, 87.5% had a PSA level equal to or greater than 4 ng/mL at the time of diagnosis.

AJCC stage was available for 94.9% of patients in 1998 (Table 2). The majority of patients (83.1%) had localized prostate carcinoma (AJCC Stage I–II) and only 6.4% of men had documentation of advanced disease (AJCC Stage IV).

The proportion of patients with well differentiated tumors was only 9.3%, whereas 70.9% of cases were moderately differentiated (Table 2). Poorly and undifferentiated grades were documented in 19.8% of cases.

Prostate Carcinoma Presentation

Overall, 68.7% of cases were diagnosed in the absence of symptoms, including low back pain, hematuria, and/or difficulty with urination. In addition, 97.8% of asymptomatic patients had abnormal PSA values, irrespective of findings on DRE (Table 3). In terms of tumor characteristics, asymptomatic patients were more likely than symptomatic patients to have localized disease (84.6% vs. 78.2%, $P < 0.01$) and well or moderately differentiated tumors (82.2% vs. 74.6%, $P < 0.01$). Moreover, 60% of asymptomatic patients with prostate carcinoma had pretreatment PSA levels less than 10 ng/mL compared with only 49.1% of symptomatic patients. Table 4 summarizes the distribution of asymptomatic and symptomatic patients stratified by age at diagnosis, race, prostate carcinoma family history, and type of health care coverage. In general,

TABLE 3
Summary of Contemporary Prostate Carcinoma Diagnosis Based on Prostate Specific Antigen, Digital Rectal Examination, and Clinical Symptoms[a]

Characteristics	Abnormal PSA and abnormal DRE (18,755, 48.6%)	Abnormal PSA and normal DRE (18,544, 48.1%)	Normal PSA and abnormal DRE (1252, 3.2%)	Tumors (%)
Asymptomatic	12,536 (32.5%)	13,363 (34.7%)	588 (1.5%)	68.7[a]
At least one symptom	6219 (16.1%)	5181 (13.4%)	664 (1.7%)	31.3

PSA: prostate specific antigen; DRE: digital rectal examination.
[a] Summary of all patients (n = 38,551) whose pretreatment prostate specific antigen ($\geq$ 4 ng/dL) or digital rectal examination is documented as abnormal. Based on the data abstraction instrument, it was possible to confirm that pretreatment prostate specific antigen was abnormal without having the actual value of the prostate specific antigen level. Patients for whom data on prostate specific antigen, digital rectal examination, or clinical symptoms were incomplete were excluded from this analysis.

the proportion of asymptomatic patients with prostate carcinoma was higher among younger men, with abnormalities of PSA and/or DRE responsible for the diagnosis in nearly 78% of patients younger than 60 years of age. Asymptomatic patients were slightly more prevalent among white men (69.3%) than among African-American men (66.3%). Among patients with and without a family history of prostate carcinoma, 70.3% and 69.6% of newly diagnosed patients were asymptomatic, respectively. The mean age at diagnosis was younger among both asymptomatic African-American patients (65.5 years vs. 67.0 years for whites) and asymptomatic patients with a positive family history (65.2 years vs. 67.1 years for a negative family history).

Tissue Confirmation and Staging

The prostate biopsy techniques utilized in 1998 are summarized in Table 5. Needle biopsy, defined as all biopsy modalities other than TURP, was the most common method of tissue diagnosis (80.1%). At least 45.4% of biopsies were performed with TRUS guidance. In 4.2% of patients, digitally guided transrectal biopsy was performed for tissue confirmation. Twenty percent of patients were diagnosed by TURP.

Radionuclide bone scintigraphy was the most frequently employed staging modality, with 26,420 (48.7%) studies performed. Among patients who underwent a bone scan, 13% were positive for evidence of metastatic disease. CT scans were employed frequently, including pelvic CT scans in 30.5% of cases and abdominal CT scans in 28.9% of cases. Table 6 summarizes the utilization of prostate carcinoma staging modalities stratified by risk of metastatic disease. Among patients with complete data, 67.4% were classified as low risk and 37.6% as high risk for metastatic disease. For each staging modality, the proportion of patients undergoing evaluation was significantly higher among patients at high risk for metastatic disease (all P values < 0.005). Regardless of staging modality, the proportion of patients who had positive tests was significantly higher among patients at high risk for metastatic disease (all P values < 0.001).

DISCUSSION

The PCE study of prostate carcinoma provides important insight into contemporary prostate carcinoma presentation, diagnosis, and staging based on a nationwide sample of patients that includes about 40% of incident cases. Greater than 1500 hospitals contributed to the study, including community and academic medical centers from all geographic regions of the U.S. The data may be considered a national point of reference for prostate carcinoma care during the corresponding period of time.

The mean age at diagnosis (68.0 $\pm$ 8.8 years) for men with prostate carcinoma has decreased slightly, when compared with reports from 1995 (68.8 years) and 1992 (70.7 years).[2,5] This age trend has been paralleled by a migration toward a higher proportion of localized tumors of low and/or moderate grade.[1,4–7] Furthermore, this migration has been attributed primarily to the impact of widespread prostate carcinoma screening initiatives.[14,15–19] To date, however, efforts to validate, on a national level, the associations between screening and stage/grade migration have been limited to large screening studies that lacked comparable control groups.

The PCE study addressed this limitation through explicit documentation of tumor characteristics, pretreatment PSA levels, and presenting symptoms. The majority (68.7%) of patients with cancers characterized by the 1998 PCE were asymptomatic. Nearly all (97.8%) asymptomatic men with prostate carcinoma had an abnormal PSA level at the time of diagnosis. Among asymptomatic patients, isolated DRE abnormalities were exceedingly rare (2.2%). It is reasonable to speculate that most, if not all, asymptomatic patients were detected as a result of PSA-based prostate carcinoma screening initiatives. Therefore, the 1998

TABLE 4
Distribution of Asymptomatic and Symptomatic Men Stratified by Age, Race, and Prostate Carcinoma Family History[a]

Characteristics	Abnormal PSA and abnormal DRE (%)	Abnormal PSA and normal DRE (%)	Normal PSA and abnormal DRE (%)	Tumors (%)
Age (yrs)				
< 50 (*n* = 758)				
Asymptomatic	269 (35.5)	305 (40.2)	16 (2.1)	77.8
At least one symptom	89 (11.7)	73 (9.6)	6 (.8)	22.2
50–59 (*n* = 5987)				
Asymptomatic	2126 (35.5)	2407 (40.2)	96 (1.6)	77.3
At least one symptom	679 (11.3)	633 (10.6)	46 (0.8)	22.7
60–69 (*n* = 14,810)				
Asymptomatic	5032 (34.0)	5447 (36.8)	216 (1.4)	72.2
At least one symptom	2173 (14.7)	1784 (12.0)	158 (1.0)	27.8
70–79 (*n* = 14,120)				
Asymptomatic	4462 (31.6)	4583 (32.5)	217 (1.5)	65.6
At least one symptom	2517 (17.8)	2065 (14.6)	276 (2.0)	34.4
≥ 80 (*n* = 2860)				
Asymptomatic	645 (22.6)	616 (21.5)	42 (1.5)	45.6
At least one symptom	757 (26.5)	622 (21.7)	178 (6.2)	54.4
Race				
White (*n* = 31,233)				
Asymptomatic	10,431 (33.4)	10,701 (34.3)	514 (1.6)	69.3
At least one symptom	5015 (16.1)	4025 (12.9)	548 (1.8)	30.7
Black (*n* = 4771)				
Asymptomatic	1293 (27.1)	1822 (38.1)	49 (1.0)	66.3
At least one symptom	764 (16.0)	779 (16.3)	64 (1.3)	33.7
Other race (*n* = 1997)				
Asymptomatic	632 (31.6)	629 (31.5)	20 (1.0)	64.1
At least one symptom	362 (18.1)	309 (15.5)	45 (2.3)	35.9
Family history				
Negative family history (*n* = 24,105)				
Asymptomatic	8064 (33.5)	8372 (34.7)	337 (1.4)	69.6
At least one symptom	3860 (16.0)	3095 (12.8)	377 (1.6)	30.4
Positive family history (*n* = 5065)				
Asymptomatic	1803 (35.6)	1692 (33.4)	65 (1.3)	70.3
At least one symptom	832 (16.4)	631 (12.5)	42 (0.8)	29.7
Primary insurance				
Private insurance (*n* = 6400)				
Asymptomatic	2215 (34.6)	2450 (38.3)	87 (1.4)	74.3
At least one symptom	840 (13.1)	736 (11.5)	72 (1.1)	25.7
Managed care (*n* = 9477)				
Asymptomatic	3427 (36.2)	3559 (37.6)	145 (1.5)	75.2
At least one symptom	1218 (12.9)	1034 (10.9)	94 (1.0)	24.8
Medicare (*n* = 18,639)				
Asymptomatic	5677 (30.5)	6117 (32.8)	258 (1.4)	64.7
At least one symptom	3286 (17.6)	2856 (15.3)	445 (2.4)	35.3
Veterans Administration (*n* = 2300)				
Asymptomatic	712 (31.0)	687 (29.9)	10 (0.4)	61.3
At least one symptom	572 (24.9)	296 (12.9)	23 (1.0)	38.7

PSA: prostate specific antigen; DRE: digital rectal examination

[a] Summary of results for patients for whom data on pretreatment prostate specific antigen, digital rectal examination, clinical symptoms, and relevant covariates (i.e., age, race, family history, insurance) were complete.

PCE may provide novel insight into the current status of prostate carcinoma screening in the U.S.

It is has been proposed that screening based on PSA is associated with a higher proportion of clinically and pathologically localized tumors.[14,15,17,18] A recent analysis compared the pathologic stage and grade of tumors detected by PSA-based screening to historical cancers detected by needle biopsy or TURP.[19] The authors found that screen-detected cancers were more likely to be pathologically organ confined and

TABLE 5
Distribution of Prostate Biopsy Modalities

Characteristics	No. of subjects	Subjects (%)
Biopsy modality	(n = 45,816, 84.5%)	
TRUS biopsy	20,816	45.4
TURP	9117	19.9
Needle biopsy, NOS	6508	14.2
Digital transrectal biopsy	1917	4.2
Perineal biopsy	379	0.8
Cytology	118	0.3
Combination	2659	5.8
Biopsy, NOS	4302	9.4

TRUS: transrectal ultrasound; TURP: transurethral resection; NOS: not otherwise specified.

less likely to be Gleason score 8–10 tumors. Nonetheless, a perennial limitation of such investigations is the need for historical comparisons, rather than assessment of a concurrent population of cancers detected for indications other than screening based on PSA levels. In contrast, the 1998 PCE identifies a large, contemporary sample of patients with pertinent symptoms (difficulty urinating, low back pain, and/or hematuria) at the time of prostate carcinoma diagnosis, thereby providing a more valid control group. Overall, 31.3% of patients reported one or more symptoms at the time of diagnosis. Despite the high prevalence of PSA abnormalities (95%) in these patients, it seems reasonable to contend that the presence of symptoms disqualifies PSA as a screening tool in these patients.

Therefore, this is the first national study to allow coincident comparison of asymptomatic patients and patients with clinically diagnosed tumors and provides the first nationwide data supporting an association between asymptomatic (screen detected) patients and favorable stage and grade migrations. These observations are consistent with recent data from the European Randomized Study of Screening for Prostate Cancer.[20] The European study demonstrated more favorable stage and grade outcomes among screen-detected versus clinically diagnosed prostate carcinomas. If, as suggested by several investigators, treatment of organ-confined cancers ultimately manifests a survival benefit, then these findings may lend additional credence to the premise that screening will ultimately decrease prostate carcinoma mortality.[17,18,21–24]

These data also allow novel observations regarding nationwide patterns of prostate carcinoma screening in the context of age, race, family history, and health care insurance. Current recommendations for prostate carcinoma screening vary between different medical specialties and professional organizations.[12,25] The ACS and the American Urological Association (AUA) continue to recommend screening with PSA and DRE for all men older than 50 years of age, whose life expectancy is at least 10 years. Initiation of screening at a younger age (40–45 years) is advocated for patients at increased risk, including African-American males and patients with a first-degree relative diagnosed with prostate carcinoma. We observed that greater than 70% of men younger than 70 years of age were asymptomatic. This proportion decreased to 65.6% in the 70–79-year-old age group and declined further to 45.6% among men older than 80 years of age. Although the prevalence of asymptomatic patients is higher among younger men who are more likely, on average, to benefit from early detection, it is noteworthy that among men 80 years and older, nearly one-half of men were asymptomatic and, therefore, prostate carcinoma was likely to be detected by screening. This finding is plausible in light of reports describing contemporary practice patterns of both urologists and primary care physicians, many of whom continue routine PSA testing in patients older than 80 years of age.[26,27]

Both the ACS and the AUA advocate commencement of screening at a younger age among African-American men and patients with a positive family history. In the 1998 PCE, the proportion of asymptomatic men with prostate carcinoma was similar among African-Americans (66.3%) and whites (69.3%). However, the mean age at diagnosis was slightly younger for asymptomatic black men (age 65.5 years vs. age 67 years). Although this finding suggests an important trend toward earlier diagnosis of cancers in asymptomatic blacks, the results of two recently published studies comparing blacks and whites with screen-detected cancers fail to support this hypothesis.[28,29] Similarly, patients with a positive family history were younger (65.0 years) at the time of diagnosis than patients with no affected relatives (67.1 years), although the proportion of asymptomatic patients was similar for these two groups (70.3% vs. 69.6%).

In terms of insurance coverage, the highest proportions of asymptomatic men were detected among patients enrolled in managed care plans and among those with private health insurance. This finding is consistent with a greater emphasis on preventative health measures among commercial insurance plans versus Medicare and/or Veterans Administration coverage.

The results of the current study suggest a central role for PSA-based screening in the contemporary diagnosis of prostate carcinoma. However, significant controversy remains regarding the clinical significance of tumors detected by screening initiatives.[16,17,30] Several clinicopathologic parameters in-

TABLE 6
Diagnostic Modalities for Evaluating Extent of Disease Stratified by Pretreatment Prostate Specific Antigen and Tumor Grade

PSA and grade criteria	Bone scan	CT of the abdomen	CT of the pelvis	MRI	PLND
Low-risk category (21,063, 67.4)					
PSA ≤ 10 ng/mL and low–moderate grade	10,047[a]	5108[a]	6272[a]	872[a]	5473[a]
	47.7[b]	24.3[b]	29.8[b]	4.1[b]	26.0[b]
	7.9[c]	11.5[c]	17.9[c]	50.5[c]	9.4[c]
High-risk category (10,177, 32.6)					
PSA > 10 ng/mL and/or high grade	6132[a]	3389[a]	3567[a]	700[a]	2802[a]
	60.4[b]	33.4[b]	35.2[b]	6.9[b]	27.6[b]
	21.7[c]	31.0[c]	33.2[c]	72.3[c]	35.9[c]

PSA: prostate specific antigen; CT: computed tomography; MRI: magnetic resonance imaging; PLND: pelvic lymph node dissection.
[a] Number of studies.
[b] Percentage of cases with test performed.
[c] Percent positive.

cluding serum PSA levels, histologic grade, and tumor stage have been reported to correlate with the biologic aggressiveness of individual prostate carcinomas.[25,31–35] Among patients with comprehensive data, 68.7% of reported cancers were found in asymptomatic patients and, thus, ostensibly detected by screening with either PSA and/or DRE. As a result, assessment of the PSA levels and histologic grades of asymptomatic (screen-detected) patients with prostate carcinoma may provide insight regarding their clinical significance. In terms of grade, 92.4% of asymptomatic patients had tumors that were moderately (Grade 2), poorly (Grade 3), or undifferentiated (Grade 4) and were therefore associated with greater biologic aggressiveness.[36] In addition, 88% of asymptomatic patients had PSA levels equal to or greater than 4 ng/mL, a finding typically associated with more clinically significant cancers, as well as a greater likelihood of extraprostatic extension.[30] Furthermore, PSA levels higher than 20 ng/mL were detected in 15.3% of asymptomatic patients. This degree of PSA elevation has been associated with an 80% risk of non–organ-confined disease and at least a 15% chance of tumor involvement of the seminal vesicles or pelvic lymph nodes.[30] In this context, the PSA and grade data suggest that many of the asymptomatic cases from the 1998 PCE are clinically significant lesions based on their potential for biologic aggressiveness.

Data from the 1998 PCE allow several observations regarding contemporary prostate biopsy techniques. The current standard for prostate carcinoma pathologic diagnosis is TRUS-guided needle biopsy of the prostate .[37] In 1998, only 45.4% of reported patients underwent TRUS-guided biopsy for pathologic diagnosis. An additional 14.2% of patients underwent prostate needle biopsy. However, for these patients, explicit documentation regarding utilization of radiographic guidance is not available. TURP (19.8%) remains a common alternative method of tissue diagnosis. Overall, a significant number of patients may be obtaining a tissue diagnosis by techniques other than TRUS-guided biopsy and further studies and/or refinement of the PCE data abstraction tool may be necessary to clarify the indications for these alternative approaches. As current trends in prostate biopsy evolve, explicit evaluation of the number and location of prostate biopsy cores, the percent of cancer in each core, as well as the use of local anesthetic will enhance the relevance of future patient care evaluations.[37,38]

In addition to patterns of diagnosis, data from the 1998 PCE also characterize contemporary utilization of prostate carcinoma staging modalities. In 1998, the most commonly employed staging modality was radionuclide bone scan in about 48.7% of patients. In addition, nearly 30% of patients underwent staging CT and/or pelvic lymphadenectomy. Although the utilization of these staging modalities was relatively frequent, the yield was fairly low. For each staging modality, with the exception of MRI scans, less than one in three patients evaluated had abnormal findings suggestive of cancer.

The utilization of staging evaluations was evaluated in the context of disease risk to determine baseline estimates of nationwide staging practices before the publication and dissemination of formal guidelines.[12,13,25] Our findings were somewhat encouraging, in that, for each staging modality, the proportion of patients tested, as well as the proportion of positive tests, was uniformly greater in the high-risk group (Table 6). However, radiographic and/or surgical staging of high-risk patients was not universal. In addition, a significant proportion of patients in the low-risk group may have undergone unnecessary staging evaluations. Nearly one-half of the low-risk patients re-

ceived bone scans and approximately one-third underwent cross-sectional imaging. Although the potential for mitigating clinical circumstances is acknowledged, strict adherence to recently published guidelines would render most of these staging evaluations unnecessary.[12,13,25] This observation is consistent with a recent update from the CaPSURE database that evaluated the use of staging modalities with even greater resolution.[39] In that study, the investigators used PSA, Gleason sum, and clinical stage to classify patients into low, intermediate, and high-risk groups for analysis of imaging test utilization. Similar to these results, the authors concluded that although staging is more frequent among high- risk cases, it is not performed uniformly. Similarly, many patients at low and intermediate risk for metastatic disease underwent unnecessary testing.[39] Therefore, nonselective staging practices may be a persistent dilemma among urologists.[40] An explanation for this finding is not readily apparent and certainly merits evaluation in future studies.

Although the findings from the current study provide an important characterization of contemporary approaches to prostate carcinoma diagnosis and staging, there are several limitations of these data that merit discussion. Although the NCDB represents a large, nationwide sample, including both community and academic medical centers, the enormous volume of data in this repository precludes audit and verification of all reports. Therefore, a finite number of data errors are unavoidable. In addition, the selection of hospitals for the NCDB is not based on systematic sampling. Therefore, a perennial limitation of this data set is the underrepresentation of diagnostic and treatment encounters occurring outside the hospital setting. In this framework, however, the study still evaluated approximately 40% of incident cases of prostate carcinoma. Despite these limitations, prostate carcinoma data from the NCDB has been compared with population-based information from the SEER program and has been shown to be similar, further establishing its role as a national point of reference.

Another limitation includes the use of the combined staging system. In this context, the risk of understaging is potentially significant because the true extent of disease is uncertain except among patients treated with radical prostatectomy. However, the uniform application of this staging system across different regions and patient populations may limit its impact on the validity of our observations. Similar concerns may be raised for the grading system, including the use of a combination of biopsy and prostatectomy tumor grades. The reported observations may be limited by the absence of Gleason sum as the primary grading system, given the prevalence of this classification in contemporary prostate carcinoma research and clinical practice. Nonetheless, the grading system in the PCE study is similar to that utilized in previous reports from the NCDB and therefore provides a basis for comparative analyses. This analysis may also be criticized for equating asymptomatic tumors (associated with abnormalities of PSA and/or DRE) with screen-detected lesions. However, although the 1998 PCE provides no explicit data concerning the use of screening, one may reasonably infer that the diagnosis of prostate carcinoma in an asymptomatic patient with an elevated PSA level and/or abnormal DRE was prompted by one or both of these screening modalities. In addition, we recognize that the observations regarding prostate carcinoma screening are limited by a lack of data regarding the number of men who were screened and did not have cancer. Finally, this analysis does not address treatment patterns or survival among this patient cohort. The absence of these data limits the significance of the observed association between asymptomatic cancers and lower stage and grade. In other words, this finding has little clinical value in the absence of appropriate therapeutic intervention. Fortunately, corresponding treatment data are available for this patient population and will be described in pending communications from the NCDB. Ultimately, data from established randomized, controlled trials of prostate carcinoma screening will provide the strongest evidence for an impact of screening on mortality.[41,42] Once survival data are available for this cohort of patients in 2003, correlation of survival outcomes among symptomatic versus asymptomatic cancers may provide preliminary insight on the nationwide impact of screening on mortality from prostate carcinoma.

Conclusions

In 1998, most newly diagnosed prostate carcinomas were of localized stage and moderate grade. A high proportion of tumors were detected in asymptomatic men with elevated PSA levels and/or abnormal findings on DRE, suggesting a principal role for prostate carcinoma screening. Asymptomatic cancers were diagnosed at a younger age in African-American men and in men with a pertinent family history, potentially reflecting adherence with current guidelines for prostate carcinoma screening. Compared with symptomatic patients, cancers in asymptomatic men were more likely to be organ confined and well or moderately differentiated. This finding provides the first demonstration, in a nationwide sample, of favorable stage and grade outcomes among screened versus symptomatic patients, diagnosed in the same time

interval. Whether these findings reflect a potential survival benefit will require future correlation with, as yet unavailable, mortality data.

TRUS-guided prostate biopsy is the most common method of pathologic diagnosis, although utilization of this technique is certainly not universal. Although radiologic and surgical staging is more common among patients at increased risk for extraprostatic disease, a substantial fraction of high-risk patients may not receive sufficient evaluation of their disease burden. In addition, more selective use of staging studies among patients at low risk for disseminated disease is desirable. The observations in the current study provide a national point of reference for evaluating current methods of prostate carcinoma diagnosis and staging.

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