Contemporary Population-Based Comparison of Localized Ductal Adenocarcinoma and High-Risk Acinar Adenocarcinoma of the Prostate

Vignesh T. Packiam, Sanjay G. Patel, Joseph J. Pariser, Kyle A. Richards, Adam B. Weiner, Gladell P. Paner, David J. VanderWeele, Gregory P. Zagaja, and Scott E. Eggener

OBJECTIVE To compare pathological characteristics, treatment patterns, and survival in patients with ductal adenocarcinoma (DC) compared to those with acinar adenocarcinoma (AC).

MATERIALS AND METHODS Using the National Cancer Database, we identified patients diagnosed with clinically localized (cN0, cM0) pure DC (n = 1328) and AC (n = 751,635) between 1998 and 2011. High-risk AC was defined as Gleason 8-10. Demographic, treatment, pathological, and survival characteristics of patients were compared.

RESULTS Compared to patients with Gleason 8-10 AC, those with DC presented with lower mean prostate-specific antigen (10.3 vs 16.2 ng/mL, $P < .001$), had similar rates (11.7% vs 11.5%, $P = .8$) of clinical extra-capsular extension (stage $\geq$ cT3), and were more likely to undergo prostatectomy (54% vs 36%, $P < .001$). Compared to patients with Gleason 8-10 AC undergoing prostatectomy, those with DC had more favorable pathology: stage $\geq$ T3 (39% vs 52%, $P < .001$), fewer positive lymph nodes (4% vs 11%, $P < .001$), and fewer positive margins (25% vs 33%, $P < .001$). On Kaplan-Meier analysis, patients with DC had similar 5-year survival (75.0%, 95% confidence interval [CI] [71.7-78.9]) compared to those with Gleason 8-10 AC (77.1%, 95% CI [76.6%-77.6%], $P = .2$). On Cox multivariable analysis, patients with Gleason 8-10 AC had a similar risk of death compared to those with DC (hazards ratio = 0.92, 95% CI [0.69-1.23], $P = 6$).

CONCLUSION In this large contemporary population-based series, patients with DC of the prostate presented with lower prostate-specific antigen, had more favorable pathological features, and similar overall survival compared to men with Gleason 8-10 AC. UROLOGY 86: 777–782, 2015. © 2015 Elsevier Inc.

Acinar adenocarcinoma (AC) represents the vast majority of prostate cancers with the remaining 5%-10% comprising a variety of other histologic subtypes. Ductal carcinoma (DC) comprises ~5% of all prostate cancers.[1] Some initial reports considered DC to portend a more favorable prognosis.[2] Multiple small series subsequently demonstrated more aggressive features associated with DC.[3-6] In an update to the Gleason scoring system in 2010, Epstein favored defining these tumors as Gleason 4+4 while retaining the nomenclature of ductal to highlight differences compared to conventional acinar tumors.[7] More recently, 2 large studies of the SEER database demonstrated DC is associated with advanced disease at presentation, increased risk of mortality when compared to all patients with AC, and has a similar prognosis to high-risk AC.[8,9]

Although there is general consensus that DC is more aggressive than AC, there is not necessarily agreement pertaining to recommended treatment modalities.[10] Studies have shown varying efficacy for hormone therapy (HT),[2,10-12] radiation treatment (RT),[10,13,14] and radical prostatectomy (RP).[3,4] These discrepancies are likely to be influenced both by differences in delivery of treatment between older and more recent literatures, as well as the small size of most series. The controversies surrounding optimal treatment for this rare histologic subtype were a primary incentive for utilizing a large series

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

From the Section of Urology, Department of Surgery, University of Chicago, Chicago, IL; the Department of Urology, University of Wisconsin-Madison, Madison, WI; the Pritzker School of Medicine, University of Chicago, Chicago, IL; the Department of Pathology, University of Chicago, Chicago, IL; and the Department of Medicine, University of Chicago, Chicago, IL

Address correspondence to: Vignesh T. Packiam, M.D., The University of Chicago, 5841 South Maryland Ave. MC-6038, Chicago, IL 60637. E-mail: vignesh.packiam@uchospitals.edu

Submitted: April 14, 2015, accepted (with revisions): July 3, 2015

Table 1. Demographic and clinical characteristics of patients by tumor type

Parameter	DC (%)	AC Gleason 6-7 (%)	AC Gleason 8-10 (%)	*P*-Value
Number of patients	1328 (0.2)	664,987 (88.3)	86,648 (11.5)	
Age (y)				<.001
<65	523 (39)	349,788 (53)	29,374 (34)	
65-75	504 (38)	252,504 (38)	36,322 (42)	
>75	301 (23)	62,695 (9)	20,952 (24)	
Ethnicity				<.001
White	1096 (82.5)	543,242 (81.7)	69,995 (80.8)	
Black	156 (11.8)	89,188 (13.4)	12,013 (13.9)	
Other	53 (4.0)	17,271 (2.6)	3041 (3.5)	
Unknown	23 (1.7)	15,286 (2.3)	1599 (1.8)	
Charlson comorbidity index				<.001
None	875 (82.4)	570,996 (85.9)	72,451 (83.6)	
1	160 (15.1)	81,809 (12.3)	11,840 (13.7)	
2	27 (2.5)	12,182 (1.8)	2357 (2.7)	
Distance from hospital				<.001
Same zip code	42 (3.2)	18,838 (2.8)	2873 (3.3)	
<60 miles	1043 (78.5)	549,718 (82.7)	73,173 (84.5)	
>60 miles	91 (6.9)	38,690 (5.8)	4254 (4.9)	
>120 miles	152 (11.4)	57,741 (8.7)	6348 (7.3)	
Geographic location				<.001
Northeast	276 (20.8)	142,837 (21.5)	18,060 (20.8)	
South/Southeast	322 (24.2)	188,927 (28.4)	22,998 (26.6)	
Midwest	325 (24.5)	177,143 (26.6)	23,340 (26.9)	
West	405 (30.5)	156,080 (23.5)	22,250 (25.7)	
Location				<.001
Metro	1045 (82.4)	518,498 (81.7)	67,079 (80.9)	
Urban	186 (14.7)	100,723 (15.9)	13,673 (16.5)	
Rural	37 (2.9)	14,944 (2.4)	2116 (2.6)	
Year of diagnosis				<.001
1998-1999	80 (6.0)	0†	0†	
2000-2003	258 (19.5)	0†	0†	
2004-2007	416 (31.3)	338,871 (51.0)	42,666 (49.2)	
2008-2011	574 (43.2)	326,116 (49.0)	43,982 (50.8)	
PSA at diagnosis*				<.001
<10	595 (74.1)	478,706 (81.3)	44,430 (57.2)	
10-20	125 (15.6)	67,478 (11.5)	17,118 (22.0)	
>20	83 (10.3)	42,327 (7.2)	16,106 (20.8)	
Clinical T stage				<.001
cT1	581 (53.5)	416,825 (70.7)	37,685 (49.1)	
cT2	377 (34.8)	160,962 (27.3)	30,219 (39.4)	
cT3	89 (8.2)	11,142 (1.9)	7690 (10.0)	
cT4	38 (3.5)	536 (0.1)	1125 (1.5)	

AC, acinar adenocarcinoma; DC, ductal adenocarcinoma.
* Mean, median, min, max, interquartile range were: 10.3, 6.3, 0.5, 74.7, [4.3-10.3] for ductal; 9.1, 5.7, 0.4, 73.5, [4.3-8.4] for Gleason 6-7; 16.1, 8.5, 0.5, 98, [5.3-16.9] for Gleason 8-10.
† Gleason score was not available for patient diagnosed prior to 2004.

in our study. We utilized the National Cancer Database (NCDB) to describe patient characteristics, patterns of treatment, and clinical outcomes in the largest contemporary cohort to date of DC of the prostate.

MATERIALS AND METHODS

We utilized the participant use file (PUF) for prostate cancer to identify our study cohort. Institutional review board exemption was not required since no patient, physician, or hospital identifiers were examined. The database utilized was developed by the NCDB, which is managed by the American College of Surgeons' Commission on Cancer and the American Cancer Society. The NCDB includes data from over 1400 approved cancer programs and captures information on approximately 70% of all cancers diagnosed in the United States.

We identified all patients diagnosed with prostate cancer on prostate biopsy between 1998 and 2011, and only included those who were diagnosed with pure, nonmetastatic (American Joint Committee on Cancer stage cM0 and cN0/cNx) DC and Gleason 6-10 AC of the prostate. Patients were stratified by histology as DC, AC Gleason 6-7, and AC Gleason score 8-10 to allow for comparison across demographic, treatment, and survival characteristics. For patients undergoing RP, it was unknown whether pathology data reflected prostate biopsy or final surgical pathology.

The NCDB comprises data initially entered at participating hospital-based cancer registries, which includes patient demographics (age, race, metropolitan urban and/or rural home county, distance traveled to cancer facility, year of diagnosis and Deyo-Charlson Comorbidity Index [CCI]),[15] cancer facility (type and location), cancer characteristics (prostate-specific antigen [PSA] and American Joint Committee on Cancer