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Original Article

Variation in surgical treatment patterns for patients with prostate cancer in the United States: Do patients in academic hospitals fare better?

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Abstract

Introduction: With prostate cancer (CaP) screening, overtreatment of low-risk CaP remains a concern. We investigated the patterns of radical prostatectomy (RP) for pathologic insignificant (iCaP) and significant CaP (sCaP) as well as variations between academic and nonacademic hospitals.

Patients and methods: Patients undergoing RP for clinical T1c CaP were identified in the National Cancer Database between 2006 and 2013. The primary outcome was the trend of RP for insignificant prostate cancer (iCaP) and significant prostate cancer (sCaP) over the study period. The secondary outcome was to compare the RP rate in academic vs. nonacademic institutions. Univariable and multivariable analysis were utilized to evaluate the association between overtreatment and practice type. iCaP was defined as organ confined CaP with Gleason Score ≤6.

Results: The total number of RP increased from 17,970 cases in 2006 to 25,324 in 2013. The RP rate decreased for iCaP from 39.9% to 19.8%, while increasing for sCaP from 18% to 27% over the study period. Patients undergoing RP in academic settings were less likely to have iCaP (odds ratio 0.88, 95% confidence interval 0.80−0.97). Caucasian race, private insurance, younger age, and treatment in the Eastern United States were associated with higher rates of iCaP at RP.

Conclusion: The rate of iCaP has declined over time in the United States for patients undergoing RP. Although RP in nonacademic setting was more likely to have iCaP on surgical pathology, this trend has been downward among practice types. Treatment appropriateness is an underrecognized, undermeasured, but increasingly important component of the high-value care discussion that warrants greater attention.

Keywords: Prostate cancer; Overtreatment; Prostatectomy

1. Introduction

The treatment of organ-confined CaP is a rapidly evolving area that is being modified constantly [1,2]. Updated results from prior randomized trials have shown increased benefit from surgical treatment over time with the Scandinavian Prostate Cancer Group Study reporting a decrease in the number needed to treat from 20 to 8 patients with proper screening [3]. This has translated to a decrease in the rate of metastasis and need for androgen deprivation therapy in similar trials [3,4]. However, CaP mortality risk reduction by surgical intervention is heavily dependent on patient and tumor characteristics with higher risk reduction in younger

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patients and higher risk groups and lower risk reduction in older patients and lower risk groups [5]. Hence, the benefits from prostatectomy should be individually estimated for each patient.

Overdiagnosis and overtreatment of CaP was an impetus for the U.S. Preventive Services Task Force recommendation against CaP screening in 2012 [6] resulting in a decline in the reported incidence of CaP [7,8]. Overtreatment has been evaluated using statistical modeling and defined as treatment of a CaP that would not ordinarily cause clinical symptoms, would not progress without treatment, would not cause death due to CaP prior to death from another cause [9]. Based on statistical modeling, it was estimated that nearly 23−42% of screen-detected prostate cancers in the United States were over diagnosed between1985 and 2000 [10].

In the current study, we investigate the changing pattern of surgical management of CaP nationally in the United States. Although this issue has been addressed previously through statistical modeling of population data [9,10], recent analysis of pathologic data from a large sample of the US population is lacking. Therefore, we utilized *pathological* outcomes in a large observational database to assess trends in patient selection and compare practice types in choosing surgical intervention for CaP. We hypothesized that the utilization of RP would decrease for insignificant CaP (iCaP) and increase for significant CaP (sCaP). We also hypothesized that the practice patterns may vary between academic and nonacademic hospitals.

2. Patients and methods

2.1. Data source

Clinicodemographic data was extracted from the National Cancer Database (NCDB), a hospital-based registry of the Commission on Cancer program of the American College of Surgeons and the American Cancer Society. This data registry captures approximately 75% of new cancer cases in the United States and is a validated database to study the delivery of care to patients with cancer [11,12]. The institutional review board at our institution exempted this study (IRB# 042503).

2.2. Study population

All patients with a diagnosis of clinical T1c prostate cancer (ICD-O-3 C61.9) were identified in the NCDB between 2006 and 2013. Patients with histology other than adenocarcinoma (code 8140) of the prostate were excluded. The cohort was limited to those who underwent open, laparoscopic, or robotic radical prostatectomy (RP). Patients with and without lymph node dissection at the time of surgery

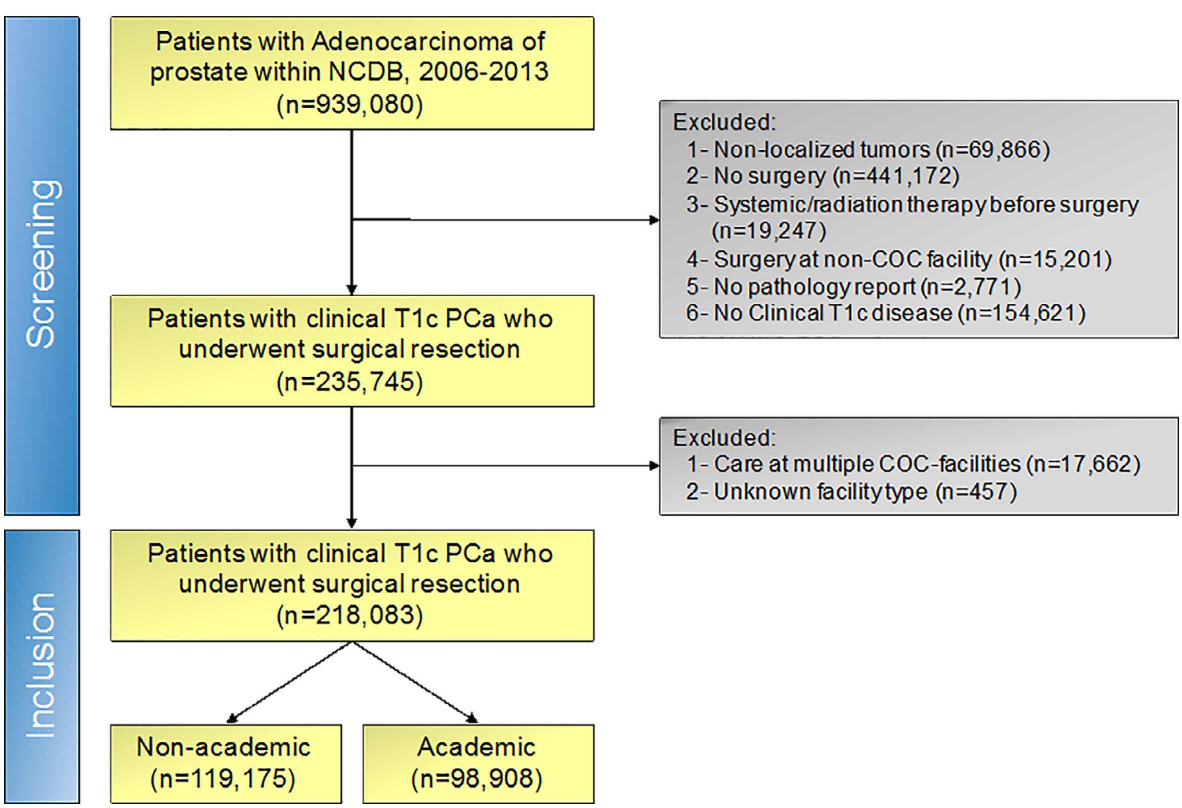

Fig. 1. Screening and inclusion process for the study.

were included. Patients with clinically nonlocalized disease (defined as cM1 or cN1) and those who received systemic therapy (chemotherapy or hormone therapy) or radiation before surgery were excluded. Patients with missing pathological staging data were also excluded.

2.3. Study variables

Our independent variable of interest was pathological iCaP at the time of RP, which is a surrogate for over treatment [13], was defined as organ confined CaP (<pT3 disease) with a pathological Gleason Score of ≤6 (any volume) and negative surgical margins. Significant CaP at the time of RP was defined as pathological Gleason Score of ≥7 or presence of nonorgan confined disease (≥pT3 disease). Clinical and pathological data were collected. Charlson-Deyo comorbidity classification was used as an indicator of comorbidities. Hospitals were categorized based on the location, surgical volume, and practice type (academic vs. nonacademic). Nonacademic hospital includes integrated cancer network, community cancer programs (100−500 new cancer cases per year), and comprehensive community cancer programs (>500 new cancer per year). Patients who received care in an unknown facility or multiple facilities were excluded. The average number of RP surgeries for each facility over the study period (by tercile) was used as yearly hospital volume. The distance between the patient and reporting hospital was defined as a great-circle distance (by mile quintiles) between the patient's residence (patient's ZIP code or the city if the ZIP code was not available) and the hospital.

2.4. Statistical analysis

The data is described with mean and standard deviation or median and interquartile ranger for continuous variables and as the frequency with percentages, where appropriate. Descriptive statistics were used to summarize clinicodemographic data. Missing data were analyzed as an independent variable [12,14]. To evaluate the association between the rate of overtreatment and receiving care in academic vs. nonacademic centers, we performed a multivariable logistic regression analysis. We included patient's characteristics and clinical data, as well as hospital's demographics as covariates. We evaluated possible interactions and multicollinearity between variables before final model assessment. Stata 15 software (Stata Corp, College Station, TX) was used. Two-tailed P values of <0.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 939,080 patients were diagnosed with CaP between 2006 and 2013, and 218,083 patients met criteria for inclusion in this study (Fig. 1). Over time the absolute number of RP for clinical T1c CaP increased from 17,970 cases to 25,324 cases from 2006 to 2013. For the full

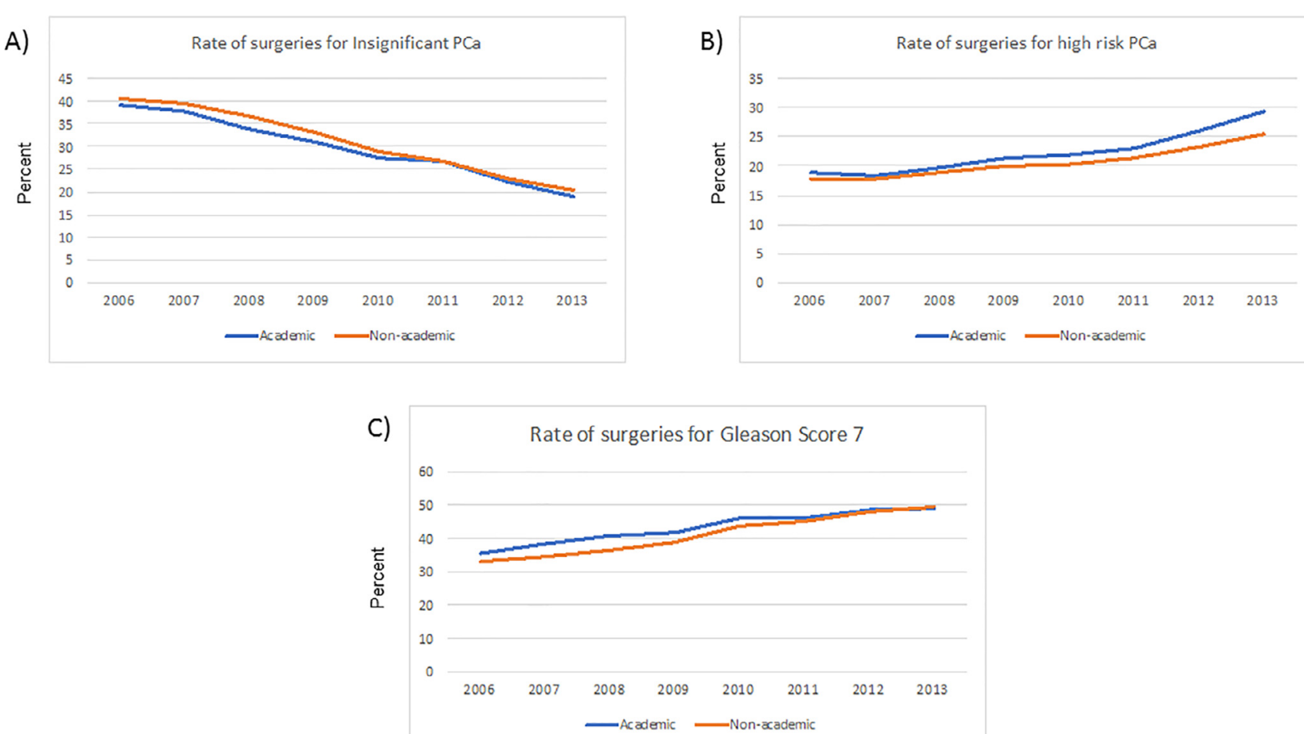

Fig. 2. Trend of RP for iCaP and significant CaP during the study period.

Table 1
Demographic and pathologic patient characteristics

	Nonacademic *N* = 119,175	Academic *N* = 98,908	*P* value
Age			<0.001
<65	79,519 (67%)	70,378 (71%)	
65−75	38,417 (32%)	27,731 (28%)	
>75	1,239 (1%)	799 (1%)	
Age at diagnosis	61 (56−66)	60 (55−65)	<0.001
Ethnicity			<0.001
White	91,255 (77%)	71,031 (72%)	
Black	12,870 (11%)	12,366 (13%)	
Hispanic/other	6,220 (5%)	6,775 (7%)	
Unknown	8,830 (7%)	8,736 (9%)	
CDCC			<0.001
0	98,485 (83%)	83,938 (85%)	
1	18,408 (15%)	13,376 (14%)	
≥2	2,282 (2%)	1,594 (2%)	
Urban/rural			<0.001
Rural	3,496 (3%)	1,238 (1%)	
Metropolitan	93,131 (78%)	83,088 (84%)	
Urban	19,222 (16%)	11,946 (12%)	
Missing	3,326 (3%)	2,636 (3%)	
Location			<0.001
East	39,318 (33%)	50,399 (51%)	
Central	56,684 (48%)	36,438 (37%)	
West	23,173 (19%)	12,071 (12%)	
Insurance status			<0.001
Medicare	36,532 (31%)	25,493 (26%)	
Private	76,849 (64%)	67,816 (69%)	
Medicaid	3,356 (3%)	3,202 (3%)	
None/Unknown	2,438 (2%)	2,397 (2%)	
Population without high-school degree in patient area (%)			<0.001
>21%	15,066 (13%)	11,546 (12%)	
13−20.9%	23,788 (21%)	17,506 (18%)	
7−12.9%	26,684 (23%)	20,622 (22%)	
<7%	49,146 (43%)	45,690 (48%)	
Income			<0.001
<$30,000	11,508 (10%)	9,172 (10%)	
$30,000−35,999	18,428 (16%)	12,749 (13%)	
$36,000−45,999	32,641 (28%)	21,498 (23%)	
>$46,000	52,116 (45%)	51,960 (54%)	
Distance			<0.001
≤5.3	28,828 (24%)	15,250 (16%)	
5.4−10.8	27,522 (23%)	15,563 (16%)	
10.9−20.4	25,435 (21%)	17,430 (18%)	
20.5−48.4	21,833 (18%)	21,519 (22%)	
≥48.5	14,748 (12%)	28,474 (29%)	
Hospital volume (cases/year)			<0.001
<39	28,474 (29%)	17,619 (18%)	
39−101	43,817 (37%)	28,464 (29%)	
>101	19,855 (17%)	52,825 (53%)	
Year of diagnosis			<0.001
2006	8,960 (8%)	9,010 (9%)	
2007	12,924 (11%)	11,695 (12%)	
2008	16,173 (14%)	13,984 (14%)	
2009	16,582 (14%)	14,553 (15%)	
2010	16,541 (14%)	13,180 (13%)	
2011	18,420 (15%)	14,169 (14%)	
2012	15,228 (13%)	11,340 (11%)	
2013	14,347 (12%)	10,977 (11%)	
PSA			<0.001
<10	90,223 (76%)	78,759 (80%)	
10−20	10,333 (9%)	8,409 (9%)	
>20	5,546 (5%)	3,925 (4%)	
Missing	13,073 (11%)	7,815 (8%)	
Biopsy GS*			<0.001
≤3+3	26,715 (41%)	21,490 (43%)	
7	24,709 (38%)	21,530 (43%)	
≥8	5,883 (9%)	4,420 (9%)	
Missing	7,229 (11%)	2,226 (4%)	
Pathologic stage			<0.001
≤pT2	96,611 (81%)	78,260 (79%)	
pT3	19,391 (16%)	18,166 (18%)	
pT4	341 (<1%)	214 (<1%)	
Missing	2,832 (2%)	2,268 (2%)	
Pathological GS			<0.001
≤6	44,878 (38%)	34,193 (35%)	
7	63,925 (54%)	56,944 (58%)	
≥8	9,014 (8%)	6,761 (7%)	
Missing	1,358 (1%)	1,010 (1%)	
Surgical margins			<0.001
Negative	93,414 (78%)	81,484 (82%)	
Positive	25,042 (21%)	16,943 (17%)	
Missing	719 (1%)	481 (<1%)	

(continued to the next column)

Table 1 (*Continued*)

* Biopsy Gleason Scores are reported for 2010−2013.

cohort, the median age was 61 (interquartile ranger 56−66), 74% of patients were Caucasian, and most patients had private insurance (66%). Nearly 36% of patients (79,071 patients) had Gleason score ≤6 disease at the time of RP. Patients were treated in nonacademic and academic centers in 54.6% and 45.4% of cases, respectively. RP was performed in 61,887 patients with insignificant CaP and 46,183 patients with high-risk CaP (GS ≥8 and/or ≥pT3a).

3.2. Primary outcome

The primary outcome was the trend of RP during the study period as well as rate of RP for pathologically insignificant and significant CaP. The total number iCaP at RP decreased from 6,453 (39.9%) cases in 2006 to 4,972 (19.8%) cases in 2013 while the number of RP for pathologically sCaP increased during the same period. Fig. 2 depicts the trend of RP for clinically iCaP and significant CaP during the study period. Significant CaP has further been subcategorized as high-risk (GS≥8 and/or ≥pT3a) and intermediate-risk (Gleason 7) CaP. The rate of pathological Gleason 7 at surgery also increased from 7,983 cases (44.4%) in 2006 to 16,547 cases (65.3%) in 2013.

3.3. Secondary outcome

The secondary outcome was RP rate in academic vs. nonacademic institutions. The total number of RP for

Table 2
Predictors of undergoing RP for insignificant CaP in multivariate analysis

Variable	Odd ratio	95% confidence interval	*P* value
Age			
<65	Referent		
65−75	0.73	0.70−0.76	<0.01
>75	0.48	0.42−0.55	<0.01
Ethnicity			
White	Referent		
Black	0.80	0.76−0.85	<0.01
Hispanic/other	0.92	0.85−0.98	0.02
Unknown	0.92	0.83−1.01	0.09
CDCC			
0	Referent		
1	0.84	0.81−0.87	<0.01
≥2	0.81	0.75−0.88	<0.01
Facility type			
Nonacademic	Referent		
Academic	0.88	0.80−0.97	0.01
Urban/rural			
Rural	Referent		
Metropolitan	1.12	1.00−1.26	0.06
Urban	1.05	0.96−1.15	0.31
Missing	1.21	1.06−1.38	<0.01
Location			
East	Referent		
Central	0.91	0.81−1.02	0.10
West	0.82	0.73−0.92	<0.01
Insurance status			
Medicare	Referent		
Private	1.13	1.09−1.17	<0.01
Medicaid	1.00	0.93−1.08	0.99
None/unknown	1.02	0.93−1.13	0.66
Population without high-school degree in patient area (%)			
>21%	Referent		
13−20.9%	1.01	0.95−1.07	0.87
7−12.9%	0.97	0.90−1.05	0.46
<7%	0.97	0.89−1.05	0.47
Income			
<$38,000	Referent		
$38,000−47,999	1.00	0.94−1.07	0.93
$48,000−62,999	1.01	0.94−1.10	0.72
>$63,000	1.04	0.95−1.14	0.37
Distance			
≤5.3	Referent		
5.4−10.8	1.01	0.97−1.06	0.53
10.9−20.4	1.00	0.95−1.04	0.86
20.5−48.4	0.98	0.92−1.04	0.48
≥48.5	1.06	0.96−1.17	0.22
Hospital volume (cases/year)			
<39	Referent		
39−101	0.95	0.88−1.04	0.27
>101	0.98	0.87−1.11	0.78
PSA			
<10	Referent		
10−20	0.57	0.54−0.59	<0.01
>20	0.67	0.61−0.74	<0.01
Missing	1.06	1.00−1.13	0.06
Year of diagnosis	0.87	0.86−0.88	<0.01

clinical T1c CaP was significantly higher in nonacademic practice compared with academic centers (119,175 vs. 98,908; *P* < 0.001). Patients' income, treatment facility location, and insurance status were factors for undergoing RP for clinical T1c CaP in academic vs. nonacademic setting (all *P* values <0.001). Patients with higher income, private insurance, and living in the Eastern US region had a higher rate of RP for clinical T1c CaP in academic practice while patients with middle income, Medicare insurance, and living in the Central and Western United States had a higher likelihood of RP in nonacademic practice. The rate of RP for clinical T1c CaP was similar among academic and nonacademic centers for lower income patients, Medicaid insurance and older patients (age >75).

Table 1 demonstrates the demographic and pathological patient characteristics during the study period per academic centers vs. nonacademic practice. The ratio of pathological insignificant (Gleason ≤6) CaP at RP was statistically higher in nonacademic practice vs. academic/research centers (44,878 (38%) vs. 34,193 (35%), *P* < 0.001). Conversely, the proportion Gleason 7 CaP on RP was significantly higher in academic/research centers compared with non-academic practice (58% vs. 54%; *P* < 0.001). The proportion for Gleason ≥8 disease was not significantly different (*P* = 0.85).

In multivariable analysis, younger age (≤65 years), Caucasian/white race, nonacademic practice, private insurance (odds ratio [OR] 1.13, 95%-confidence interval [CI] 1.09−1.17) and Eastern US in geographic region were independently associated with RP for iCaP. Conversely, patients 65−75 years of age (OR 0.73, CI 0.70−0.76), men >75 years (OR 0.48, CI 0.42−0.55), African Americans (OR 0.8, CI 0.76−0.85), Hispanics (OR 0.92, CI 0.85 −0.98), and patients with lower income (<$38,000/year) were less likely to undergo surgery for insignificant CaP (Table 2).

Multivariable analysis was performed to determine factors for pathologically sCaP at RP for clinical T1c disease. Older age (OR 1.44, CI 1.39−1.49 for men aged 65−75 and OR 2.19, CI 1.99−2.42 for men >75), Hispanic race and Charlson-Deyo comorbidity classification 1 (OR 1.20, CI 1.16−1.24) and ≥2 (OR1.32, CI 1.22−1.43) were associated with significant disease on final pathology (Table 3). Patients with private insurance were less likely to have significant disease when undergoing RP (OR 0.90, CI 0.87 −0.94).

3.4. Exploratory analysis

In this database, 52,998 men with clinical T2 and 5,909 men with clinical T3 disease underwent RP between 2006 and 2013. Insignificant cancer was found in 24% and 0.7% of patients with clinical T2 (28% for T2a, 13% for T2b, and 25% for T2c) and T3 disease, respectively. The rate of

Table 3
Predictors of significant CaP in multivariate analysis

Variable	Odd ratio	95% confidence interval	*P* value
Age			
<65	Referent		
65−75	1.44	1.39−1.49	<0.01
>75	2.19	1.99−2.42	<0.01
Ethnicity			
White	Referent		
Black	1.00	0.94−1.06	0.99
Hispanic/other	1.08	1.02−1.15	0.01
Unknown	1.06	0.96−1.18	0.26
CDCC			
0	Referent		
1	1.20	1.16−1.24	<0.01
≥2	1.32	1.22−1.43	<0.01
Facility type			
Nonacademic	Referent		
Academic	1.07	0.97−1.19	0.19
Urban/rural			
Rural	Referent		
Metropolitan	1.06	0.97−1.17	0.21
Urban	1.06	0.96−1.16	0.24
Missing	0.98	0.87−1.11	0.78
Location			
East	Referent		
Central	0.98	0.89−1.08	0.68
West	0.95	0.85−1.07	0.43
Insurance status			
Medicare	Referent		
Private	0.90	0.87−0.94	<0.01
Medicaid	1.00	0.93−1.07	0.98
None/Unknown	1.11	1.01−1.22	0.03
Population without high-school degree in patient area (%)			
>21%	Referent		
13−20.9%	0.96	0.92−1.01	0.09
7−12.9%	1.00	0.94−1.06	0.93
<7%	0.93	0.87−0.99	0.04
Income			
<$38,000	Referent		
$38,000−47,999	0.96	0.91−1.01	0.14
$48,000−62,999	0.96	0.91−1.02	0.18
>$63,000	0.96	0.90−1.03	0.27
Distance			
≤5.3	Referent		
5.4−10.8	0.98	0.94−1.02	0.27
10.9−20.4	0.96	0.92−0.99	0.04
20.5−48.4	1.00	0.95−1.05	0.94
≥48.5	1.02	0.95−1.10	0.58
Hospital volume (cases/year)			
<39	Referent		
39−101	1.04	0.97−1.11	0.26
>101	1.18	1.04−1.34	0.01
PSA			
<10	Referent		
10−20	2.41	2.32−2.49	<0.01
>20	2.47	2.28−2.68	<0.01
Missing	1.01	0.95−1.08	0.68
Year of diagnosis	1.07	1.06−1.08	<0.01

insignificant cancer at surgery for men with clinical T2 disease was decreased from 34% in 2006 to 15% in 2013. The rate of finding insignificant cancer in men with clinical T2 disease is more frequent in nonacademic centers compared with academic centers (26% vs. 22%, *P* value <0.01).

5. Discussion

Overdiagnosis and overtreatment of patients with indolent prostate cancer may have been a primary impetus behind the U.S. Preventive Services Task Force recommendation against PSA screening in 2012. However, several recent modifications to the management of this disease have led to reduced treatment of clinically iCaP [15,16]. While several studies have investigated this trend, few utilized pathologic data to evaluate the effect of treatment refinements. In our current study we evaluate trends in RP for pathologically iCaP and correlate this with clinicodemographic predictors. Our study has several important findings. First, we show a decrease in the absolute number of RP for pathologic iCaP and an increase in the number of RP for sCaP. Also of importance is the absolute number of RPs have gone up. We are doing more RPs now than before. Second, we show that practice type is significantly associated with the surgical management of CaP, specifically in terms of likelihood of RP for clinically iCaP. Lastly, patient factors influenced the utilization of RP for clinically iCaP.

Statistical models have estimated that up to 23−42% of screen detected CaP in the United States has been overtreated between 1985 and 2000 [10]. This includes patients undergoing treatment for organ confined GS <7 regardless of tumor volume based on the contemporary concept of insignificant CaP [17]. However, the estimates based on statistical modeling have been deemed imperfect and biased since a portion of the PSA screening tests included in the models were actually performed after CaP diagnosis. On the other hand, clinicopathologic data from studies on surgically treated patients have reported the rate of overdiagnosis in the range of 5−20% [18,13] and suggest that the epidemiologic estimates of overdiagnosis of CaP might be exaggerated. In our study, The rate of RP for iCaP was 39.9% at 2006 and decreased to 19.8% in 2013. The observed trends demonstrated in Fig. 1 may reflect the implementation of the current recommendations to refrain from overtreatment of low-risk disease among urologists as the side effects and morbidity of surgery may outweigh the benefits. The decline in overtreatment of iCaP might also be the result of a decrease in overdiagnosis of CaP as the incidence of early stage CaP has substantially declined since 2011 based on data from large representative cohorts [7]. Additionally, improved risk stratification using nomograms, genomic tests, and multiparametric MRI might have played a role in the downward trend of surgical overtreatment of iCaP [19].

The upward trend of RP for high-risk CaP may be the result of improvements in surgical technique including using visual cues to identify poorly defined planes or appearance of prostate tissue on the neurovascular bundle, widespread access to robotic surgery, and the urologists' belief that RP may be more beneficial in this high-risk population [20]. Similar analyses from several European institutions have reported a relative decrease in the fraction of patients with low-risk disease in patients treated with RP patients [16,21]. Our study identifies comparable findings in a US cohort and examines the distribution of RP for pathologic insignificant and significant disease among urology practice type and patient characteristics.

In a national survey, Kim et al. reported significant differences in physician perception and management recommendations for low-risk CaP [22,23], reporting specialty bias in treatment recommendations among urologists and oncologists for localized CaP. They reported that physicians practicing in academic centers had a higher odds of recommending active surveillance when compared with those practicing in a community setting. Although our study did not investigate utilization of active surveillance, we do show that patients undergoing RP in academic centers were less likely to have pathologically insignificant CaP. This might stem from assigning more CaP patients to active surveillance in academic centers as observed in previous studies or might be justified by tertiary referral based nature of academic centers and hence, managing higher rates of clinically significant CaP. Furthermore, while differences in rates of iCaP at RP were statistically different between academic and nonacademic centers, an overall 3% absolute difference may not be clinically meaningful.

Our study demonstrates that factors other than tumor characteristics may play an important role for undergoing surgical treatment for CaP. In our study, African American (AA) and Hispanic men were less likely to have pathologically iCaP following RP and therefore, were less likely to be overtreated. This can be at least partially explained by a higher rate of pathologic upstaging of low-risk CaP in AAs [24]. Similar studies have also reported racial disparities with higher rates of upstaging and adverse pathologic outcomes for AA men undergoing RP for low and very low-risk CaP [25,26]. This is contrary to a study from UCSF that did not find significant rates of upstaging and upgrading for AA men who underwent RP for low-risk CaP [27]. Additionally, we found that men with higher income were not any more likely to undergo RP for iCaP. This is similar to the nationwide study of National CaP Registry of Sweden that reported no significant difference in active treatment for very low-risk CaP between highest and lowest socioeconomic class [28].

The findings in our study should be interpreted within the context of another population-level analysis of CaP treatment trends by Borza et al. [29], who concluded that the decline in CaP treatment observed from 2006 to 2012 was due to changes in attitudes and behaviors surrounding screening and diagnosis rather than greater restraint by specialists once CaP was diagnosed. In this report, the likelihood of radical treatment for CaP in men at the highest risk of non-CaP death and regional variation in treatment rates remained unchanged, suggesting that overtreatment has likely persisted, at least during the time-frame analyzed. However, our study provides some reassuring evidence that this overall stable trend may be the result of a shift in the CaP-risk profile of men undergoing RP from lower to higher risk. In addition to a greater understanding of the behavior of low-risk CaP and a more widespread acceptance of active surveillance, improved risk stratification using nomograms, genomic tests, and multiparametric MRI have improved our ability identify appropriate candidates for radical treatment and permit a more refined evaluation of risks and benefits. The declining trend in CaP diagnosis has continued since 2011, based on Surveillance, Epidemiology, and End Results data [7], leaving open the possibility that specialists have made additional progress curtailing overtreatment.

Our findings must be interpreted within the limits of the study. First, the retrospective nature gives rise to omitted variable biases that may not be accounted for despite our attempts to control for known confounding factors using multivariable logistic regression and covariate adjustments. Second, the NCDB only contains data from Commission on Cancer-accredited hospitals, and therefore, our findings may not be generalizable to nonparticipating sites. Third, several patients and cancer specific characteristic are not available in the NCDB, which may have affected our analysis. For example, information regarding the type of biopsy and number/percentage of positive cores at biopsy was not available prior to 2010. Additionally, the incidence and characteristics of patients with CaP who underwent active surveillance, watchful waiting, radiation, or focal therapy were not included in our analysis. In addition, NCDB lacks data on subsequent adjuvant/salvage therapies as well as cancer-specific mortality data, thought those were not outcome measures in our study.

Despite these limitations, our study demonstrates decreasing utilization of RP for pathologically iCaP among varying practice types and over time, which is congruent with the implementation of the guideline recommendations among urologists in the United States. Additionally, this study delineates the differences in surgical management of pathological iCaP per practice type with higher rates of overtreatment and positive surgical margins in a nonacademic setting. Finally, this study sheds lights on patient factors that might be associated with surgical overtreatment of CaP other than tumor characteristics.

6. Conclusion

The rate of iCaP has declined over time in the United States for patients undergoing RP. Although RP in nonacademic setting was more likely to have iCaP on surgical pathology, this trend has been decreasing among practice types (academic vs. nonacademic). A greater understanding of patient, provider, and health system factors that contribute to overtreatment is essential. Treatment appropriateness is an under-recognized, under-measured, but increasingly important component of the high value care discussion the warrants greater attention.

References

[1] Litwin MS, Tan HJ. The diagnosis and treatment of prostate cancer: a review. JAMA 2017;317:2532–42.

[2] Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2017;71:618–29.

[3] Bill-Axelson A, Holmberg L, Garmo H, et al. Radical prostatectomy or watchful waiting in early prostate cancer. N Engl J Med 2014;370:932–42.

[4] Hamdy FC, Donovan JL, Lane JA, et al. 10-Year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 2016;375:1415–24.

[5] Vickers A, Bennette C, Steineck G, et al. Individualized estimation of the benefit of radical prostatectomy from the Scandinavian Prostate Cancer Group randomized trial. Eur Urol 2012;62:204–9.

[6] Moyer VA. U S Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012;157:120–34.

[7] Jemal A, Ma J, Siegel R, Fedewa S, Brawley O, Ward EM. Prostate cancer incidence rates 2 years after the us preventive services task force recommendations against screening. JAMA Oncol 2016;2: 1657–60.

[8] Halpern JA, Shoag JE, Artis AS, et al. National trends in prostate biopsy and radical prostatectomy volumes following the US Preventive Services Task Force guidelines against prostate-specific antigen screening. JAMA Surg 2017;152:192–8.

[9] Gulati R, Inoue LY, Gore JL, Katcher J, Etzioni R. Individualized estimates of overdiagnosis in screen-detected prostate cancer. J Natl Cancer Inst 2014;106:djt367.

[10] Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. J Natl Cancer Inst 2009;101:374–83.

[11] Su C, Peng C, Agbodza E, et al. Publication trend, resource utilization, and impact of the US National Cancer Database: a systematic review. Medicine (Baltimore) 2018;97:e9823.

[12] Boffa DJ, Rosen JE, Mallin K, et al. Using the National Cancer Database for Outcomes Research: a review. JAMA Oncol 2017;3:1722–8.

[13] Pelzer AE, Bektic J, Akkad T, et al. Under diagnosis and over diagnosis of prostate cancer in a screening population with serum PSA 2 to 10 ng/ml. J Urol 2007;178:93.:7; discussion 97.

[14] Sun M, Trinh QD, Bianchi M, et al. Extent of lymphadenectomy does not improve the survival of patients with renal cell carcinoma and nodal metastases: biases associated with the handling of missing data. BJU Int 2014;113:36–42.

[15] Cooperberg MR, Carroll PR. Trends in management for patients with localized prostate cancer, 1990-2013. JAMA 2015;314:80–2.

[16] Huland H, Graefen M. Changing trends in surgical management of prostate cancer: the end of overtreatment? Eur Urol 2015;68: 175–8.

[17] Klotz L. Active surveillance: patient selection. Curr Opin Urol 2013;23:239–44.

[18] Graif T, Loeb S, Roehl KA, et al. Under diagnosis and over diagnosis of prostate cancer. J Urol 2007;178:88–92.

[19] Watson MJ, George AK, Maruf M, et al. Risk stratification of prostate cancer: integrating multiparametric MRI, nomograms and biomarkers. Future Oncol 2016;12:2417–30.

[20] Yuh B, Artibani W, Heidenreich A, et al. The role of robot-assisted radical prostatectomy and pelvic lymph node dissection in the management of high-risk prostate cancer: a systematic review. Eur Urol 2014;65:918–27.

[21] van den Bergh R, Gandaglia G, Tilki D, et al. Trends in radical prostatectomy risk group distribution in a european multicenter analysis of 28 572 patients: towards tailored treatment. Eur Urol Focus 2017.

[22] Kim SP, Gross CP, Nguyen PL, et al. Perceptions of active surveillance and treatment recommendations for low-risk prostate cancer: results from a National Survey of Radiation Oncologists and Urologists. Med Care 2014;52:579–85.

[23] Kim SP, Gross CP, Nguyen PL, et al. Specialty bias in treatment recommendations and quality of life among radiation oncologists and urologists for localized prostate cancer. Prostate Cancer Prostatic Dis 2014;17:163–9.

[24] Sundi D, Ross AE, Humphreys EB, et al. African American men with very low-risk prostate cancer exhibit adverse oncologic outcomes after radical prostatectomy: should active surveillance still be an option for them? J Clin Oncol 2013;31:2991–7.

[25] Faisal FA, Sundi D, Cooper JL, et al. Racial disparities in oncologic outcomes after radical prostatectomy: long-term follow-up. Urology 2014;84:1434–41.

[26] Ritch CR, Morrison BF, Hruby G, et al. Pathological outcome and biochemical recurrence-free survival after radical prostatectomy in African-American, Afro-Caribbean (Jamaican) and Caucasian-American men: an international comparison. BJU Int 2013;111:E186–90.

[27] Jalloh M, Myers F, Cowan JE, Carroll PR, Cooperberg MR. Racial variation in prostate cancer upgrading and upstaging among men with low-risk clinical characteristics. Eur Urol 2015;67:451–7.

[28] Tomic K, Ventimiglia E, Robinson D, Haggstrom C, Lambe M, Stattin P. Socioeconomic status and diagnosis, treatment, and mortality in men with prostate cancer. Nationwide population-based study. Int J Cancer 2018.

[29] Borza T, Kaufman SR, Shahinian VB, et al. Sharp decline in prostate cancer treatment among men in the general population, but not among diagnosed men. Health Aff (Millwood) 2017;36:108–15.