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Sociodemographic factors associated with postprostatectomy radiotherapy

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Purpose: To determine if nonclinical factors affect the use of adjuvant radiation therapy after surgical resection of the prostate gland.
Methods: Using the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) public use data files, we identified men with localized/regional prostate cancer who underwent postprostatectomy radiotherapy within 4 months of surgery. We used 2000 Census information to ascribe a median education and income level to these men based on the county of residence and ethnicity.
Results: Of 34 763 men who underwent surgical resection, 1549 received postprostatectomy radiotherapy. Those with higher tumor grade and from certain geographic regions (Seattle and Hawaii) had significantly higher rates of radiotherapy while being older and from other geographic regions (Detroit, Utah, and New Mexico) was protective. The use of additional radiation therapy was not affected by ethnicity, income level, or educational attainment.
Conclusions: We found no socioeconomic or demographic disparities in the receipt of postprostatectomy radiotherapy. Geographic variation in postprostatectomy radiotherapy may be explained by limited evidence supporting its use in clinical practice.
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Introduction

Recurrence rates following primary treatment for prostate cancer range from 5 to 30%, regardless of which therapy is chosen.[1–4] Patients deemed high risk for recurrence after primary treatment often receive adjuvant radiation therapy, defined as additional therapy administered immediately following primary treatment. Following radical prostatectomy, the presence of adverse pathologic features such as high Gleason grade, extracapsular extension, or a positive margin usually compels clinicians to advise a course of adjuvant radiation therapy.[5–7]

Adverse pathologic features in a radical prostatectomy specimen are likely the result of either aggressive tumor biology or poor patient selection. Although pretreatment PSA, Gleason score, and clinical stage are all used to predict pathologic stage and prognosis, they are not infallible.[8] Clinicians are continually evaluating novel combinations of clinical variables in a quest to improve prognostication. Nonclinical variables associated with cancer control include African American ethnicity. African Americans ethnicity has been associated with lower disease-free survival rates.[9,10] The association of ethnicity with prognosis is mitigated when researchers control for stage at presentation.[11,12] Using military rank as a surrogate for socioeconomic status, Tarman *et al*[13] found no association between socioeconomic status and biochemical recurrence rates. While many experts

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recommend postprostatectomy radiotherapy for patients with adverse pathologic factors, no data currently support such treatment on the basis of nonclinical factors. If the use of additional therapy is differentially applied on the basis of nonclinical factors such as ethnicity, education level, or income, then socioeconomic disparities in treatment exist. Since prostate cancer affects large numbers of men, discerning and alleviating such disparities would benefit many men.[14]

We used data from a national cancer registry to determine if nonclinical factors increased patient risk of postprostatectomy radiotherapy following surgical treatment of early stage prostate cancer.

Methods

Data sources

We analyzed clinical data are from the Surveillance, Epidemiology, and End Result (SEER) public use database.[15] The National Cancer Institute maintains this population-based tumor registry for 11 regions in the United States chosen to represent epidemiologically significant population subgroups. Five states (Connecticut, Hawaii, Iowa, New Mexico, and Utah) and six metropolitan areas (Detroit, San Francicso, Atlanta, Seattle, Los Angeles County, and San Jose-Monterey) comprise the 11 regions. These regions reflect the general population in terms of education and poverty level although for privacy purposes these variables are not recorded for each individual.

Study population

We identified all subjects over the age of 20 y with a SEER historic stage A code of localized/regional prostate cancer diagnosed between 1995 and 1999. Beginning in 1995, SEER collapsed all prostate cancer cases defined as 'confined entirely to the organ' or 'extended beyond the limits of the organ of origin' as determined by clinical staging into the single category of localized/regional. For each subject, the following variables were identified: county, age at diagnosis, race/ethnicity, date of diagnosis, grade, site-specific surgery, radiation, and radiation sequence with surgery. We included all patients who had radical resection of the prostate and subsequent radiation therapy. Subjects were excluded if they had radiation prior to surgery, incomplete ethnicity or grade information, or insufficient data to determine the treatment sequence. The variable *radiation subsequent to surgery* is only available for the first 4 months postdiagnosis. While many of these patients may have no evidence of disease recurrence, it is conceivable that a portion of them had a detectable PSA. Therefore, we used the more precise term postprostatectomy radiotherapy as opposed to adjuvant radiation.

Due to the lack of individual demographic data, we created two socioeconomic variables (income and education) using data from the 2000 US Census. The US Census Bureau website provides a tool called the American FactFinder that allows the user to create specific queries from the Census 2000 summary file three. We created custom tables identifying the educational attainment and median household income ($1999) for men greater than age 25 y. We further isolated men of specific ethnicity (Black alone, American Indian Alaskan Native, Asian alone, Hispanic, White alone not Hispanic, and other) residing in each of the corresponding SEER counties. The US census counties precisely matched the SEER code for county. We ascribed the median education and income level from the census data to each SEER individual based on county of residence and ethnicity.

Analysis

Descriptive statistics are presented for demographic and clinical data. Categorical variables are presented as frequencies. Logistic regression analysis was performed to investigate a link between the likelihood of adjuvant radiation treatment and demographic variables. In addition to age, geographic location and grade were included as covariates. Age remained a continuous variable in the model while income was dichotomized to less than or equal to $40 216 *vs* greater than $40 216. We categorized ethnicity as Caucasian, African American, Hispanic, and other and education level as less than high school, high school graduate, and college educated. We categorized grade as poorly differentiated, moderately differentiated, and well differentiated and specified Los Angeles as the referent SEER region.

Results

Population characteristics

Of the 104 316 subjects diagnosed with localized/regional prostate cancer during the index years, 34 763 met our inclusion criteria. Of these, 1 549 (4.5%) subjects required postprostatectomy radiotherapy (Figure 1).

Table 1 compares the characteristics of those who received postprostatectomy radiotherapy to those who did not. The subjects receiving postprostatectomy radiotherapy were slightly younger, more likely to be

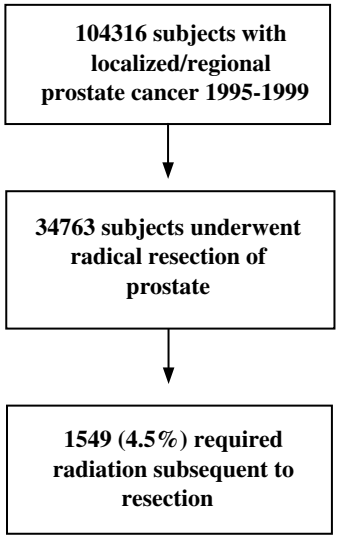

Figure 1 *Indentification of study population.*

Table 1 Demographic and clinical characteristics of patients receiving and not receiving adjuvant radiation therapy

	Adjuvant therapy n (%)	No adjuvant therapy n (%)	*P*-value
Mean age	62.4	63	0.0027
<50	1631 (4.9)	106 (6.8)	
51–60	10014 (30.2)	496 (32)	
61–70	16876 (50.8)	749 (48.4)	
>70	4693 (14.1)	198 (12.8)	
Ethnicity			
Caucasian	1173 (75.7)	25595 (77.1)	<.0001
African-American	139 (9.0)	3649 (11.0)	
Hispanic	125 (8.1)	2467 (7.4)	
Other	112 (7.2)	1503 (4.5)	
County education			
Less than high school	88 (5.7)	1688 (5.1)	0.0156
High school graduate	1045 (67.5)	23540 (70.9)	
College or beyond	416 (26.9)	7986 (24.0)	
Mean income	$51,558	$50,809	0.0262
<20,000	2 (0.1)	20 (0.1)	
20 001–40 000	338 (21.8)	7924 (23.9)	
40 001–60 000	907 (58.6)	18293 (55.1)	
>60 000	302 (19.5)	6977 (21.0)	
Grade			
Well-differentiated	31 (2.0)	1702 (5.1)	<.0001
Moderately differentiated	861 (55.6)	25598 (77.1)	
Poorly differentiated	647 (41.8)	5818 (17.5)	
Undifferentiated	10 (0.7)	96 (0.3)	
Region			
Conecticut	147 (9.5)	2735 (8.2)	<0.0001
Hawaii	61 (3.9)	557 (1.7)	
Iowa	155 (10.0)	3073 (9.3)	
New Mexico	46 (3.0)	1568 (4.7)	
Utah	54 (3.5)	2076 (6.3)	
Detroit	96 (6.2)	4428 (13.3)	
San Francisco	158 (10.2)	3167 (9.5)	
Atlanta	90 (5.8)	2034 (6.1)	
Seattle	237 (15.3)	3894 (11.7)	
Los Angeles	390 (25.2)	7797 (23.5)	
San Jose-Montery	115 (7.4)	1885 (5.7)	

Hispanic or other ethnicity ($P<0.001$), and more likely to have a college education ($P=0.01$). The most common income level for those receiving postprostatectomy radiotherapy was $40–60 000 and they were significantly more apt to have poorly differentiated ($P<0.001$) disease. Postprostatectomy radiotherapy varied substantially by geographic region with a greater propensity toward adjuvant therapy on the west coast.

Risk factors for adjuvant radiation therapy

Logistic regression modeling revealed that certain characteristics increased the risk of postprostatectomy radiotherapy (Table 2). While age was significant, older age only slightly decreased the likelihood of postprostatectomy radiotherapy (OR 0.98). However, subjects residing in the regions of Detroit (OR 0.46), Utah (OR 0.57), and New Mexico (OR 0.64) were much less likely than subjects in Los Angeles to receive postprostatectomy radiotherapy. Conversely, the subjects residing in Seattle (OR 1.39) or Hawaii (OR 1.70) were more likely to receive postprostatectomy radiotherapy. As the tumor grade worsened from moderately to poorly differentiated, the risk of adjuvant radiation therapy increased from 1.8 to 6.2. Lastly, ethnicity, income level, and educational attainment did not affect the use of adjuvant radiation.

Table 2 Multivariate analysis predicting the likelihood of adjuvant therapy

Parameter	Odds ratio	Confidence interval
Age	**0.978**	0.97–0.985
Ethnicity (vs *white)*		
African American	0.93	0.726–1.195
Hispanic	1.2	0.898–1.6
Other	1.2	0.966–1.55
Income (*vs* >$40,216)	0.92	0.752–1.114
Education (vs *College)*		
Less than high school	0.92	0.624–1.38
High school degree	0.99	0.85–1.16
Grade (vs *well-differentiated)*		
Moderately differentiated	**1.8**	1.2–2.6
Poorly differentiated	**6.2**	4.3–8.9
Region (vs *Los Angeles)*		
Detroit	**0.46**	0.36–0.59
Seattle	**1.38**	1.1–1.6
San Francisco	1.04	0.83–1.3
Connecticut	1.21	0.98–1.4
Iowa	1.14	0.91–1.4
Atlanta	0.9	0.7–1.1
Utah	**0.57**	0.42–0.76
San Jose-Monterey	1.21	0.95–1.5
New Mexico	**0.64**	0.45–0.89
Hawaii	**1.69**	1.2–2.3

Bold indicates significant findings.

Discussion

Our study suggests that socioeconomic and demographic factors do not affect receipt of postprostatectomy radiotherapy. While geographic variation persists, clinical parameters appear to be the primary determinant of adjuvant treatment. These findings differ from studies in other cancers that have assessed the influence of ethnicity, education, and income on adjuvant treatment.

Although randomized trials have shown that survival is improved with adjuvant chemotherapy combined with radiation for advanced stage colon cancer, practice patterns vary according to age and ethnicity. Analysis of the California Cancer Registry demonstrated that patients who were unpartnered, older, or African American failed to receive chemotherapy or radiation as often as their counterparts.[16] Schrag also found younger age and white ethnicity predicted adjuvant chemotherapy in colon cancer patients.[17,18] In our study, older subjects received adjuvant radiation less often but the independent effect is minimal. Ethnicity has been demonstrated to influence primary treatment rates in prostate cancer, particularly in that African American men are more likely to receive less aggressive treatment than white men.[19–21] Similarly, we found that African Americans showed a trend toward being less likely to receive postprostatectomy radiotherapy.

Surrogates for socioeconomic status—education and income—have been shown to influence adjuvant treat-

ment rates in breast cancer. A lower education level corresponded with lower adjuvant therapy rates. For example, breast-conserving treatment among women enrolled in adjuvant trials was found to be lower in those without a college degree.[22] Moreover, Gilligan *et al* noted higher adjuvant therapy rates in better-educated women. Income exhibited the same inverse effect. The residents of poorer counties were less likely to undergo breast-conserving therapy, regardless of whether it was coupled with adjuvant therapy.[23]

Studies of the impact socioeconomic variables have on adjuvant treatment in colon cancer parallel these findings.[24,25] Higher income patients, defined by per capita income at zip code level, experienced adjuvant treatment rates twice that of the lowest income patients. Having Medicare rather than private insurance also resulted in less use of adjuvant treatment.[25] While these investigators did confirm a socioeconomic gradient, other investigators have failed to demonstrate an association.[22,26–28] This disparity may be explained by investigators' use of different measures and classifications of socioeconomic position. In our study, we assigned each subject the median education and income level for men of the same ethnicity in his county of residence. Knowledge of individual educational attainment and income level would provide more precise results, however, secondary data sources rarely provide such individualized socioeconomic parameters.

Randomized controlled trials (RCT) provide the strongest evidence for clinicians to pursue a specific course of action. Even in the face of compelling findings by a RCT, dissemination and acceptance of these results takes time. Although an interim analysis of an ongoing RCT has recently been presented suggesting a benefit from adjuvant radiation therapy, clinicians during 1995–1999 faced with the management of patients with adverse pathologic features had only small retrospective analyses on which to base their recommendations.[29–32] Therefore, it is not surprising that rates of adjuvant radiation therapy varied by region. Although not all regions were significantly different, Seattle and Hawaii had increased rates of postprostatectomy radiotherapy while Detroit, Utah, and New Mexico exhibited lower rates.

These small retrospective analyses available to clinicians suggested that Gleason ≥ 8, and positive surgical margins constituted indications for adjuvant radiation therapy.[5,33] The benefit of postprostatectomy radiotherapy for seminal vesicle involvement remains controversial as 47% of patients may not experience a recurrence.[34,35] Factors found to be predictive of response to radiation postoperatively in patients with positive margins included PSA <1.0 ng/dl and Gleason <7.[31] These studies rarely included demographic variables in the analyses. Therefore, ethnicity, income, and education level cannot be considered suitable indications for postprostatectomy radiotherapy. The one parameter consistently associated with patient benefit was tumor grade. Patients with high-grade tumors (Gleason >7) appeared to experience a more durable biochemical response.[6] The strength of the odds ratio (6.2) we obtained for poorly differentiated tumors suggests that histologic grade motivated clinicians to recommend immediate postprostatectomy radiotherapy. Practice patterns appear to be consistent with the best evidence available at the time.

Our study is limited by several factors. Certain ethnicities may have had pathologic indications but did not receive adjuvant therapy. This may be due to the physician culture regarding the efficacy of postprostatectomy radiotherapy. Some geographic regions may also have lacked adequate radiation facilities. Registry data only includes preoperative parameters so this limitation is difficult to address. We further are assuming that subjects received adjuvant therapy for the aforementioned reasons and that the lack of radiation therapy suggests equivalent patient selection. However, it is possible that adverse pathologic characteristics were treated with hormone ablation or that imaging diagnosed occult metastasis. Finally, while using census data overcomes the obstacle presented by the lack of individual demographic data in SEER, it is limited by ecologic fallacy. Further studies using a database that includes individual data, rather than ascribing group data to individuals are needed to confirm or refute our findings.

Conclusion

Nonclinical factors, with the exception of geographic region, did not affect the use of postprostatectomy radiotherapy following surgical treatment of early stage prostate cancer. Receipt of adjuvant treatment appears to be based primarily on the pathologic features in accordance with the literature.

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