

Scientific Article

Regional Differences in the Treatment of Localized Prostate Cancer: An Analysis of Surgery and Radiation Utilization in the United States



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Received 9 October 2018; accepted 13 January 2019

Abstract

Purpose: Men with localized prostate cancer have various treatment options available in their management. The optimal approach is controversial and can be influenced by multiple factors. This study aimed to investigate the influence of geographic region on the selection of treatment for prostate cancer.

Methods and Materials: Using the National Cancer Database, we identified men diagnosed with localized prostate cancer between 2010 and 2014. The United States was divided into 11 regions per the American Cancer Society Divisions. The first course of treatment was recorded as radiation therapy (RT), radical prostatectomy (RP), or active surveillance (AS). The RT subgroup consisted of patients receiving all forms of RT, including external beam and brachytherapy, or RT plus androgen deprivation therapy. The RP subgroup consisted of patients receiving RP alone or combined with RT or androgen deprivation therapy. A χ^2 test was performed to assess the association between region and frequency of RT and RP.

Results: This study included 462,811 men with localized prostate cancer who were treated in the United States, of whom 63.46% underwent RP, 31.54% underwent RT, and 5.00% underwent AS. Significant regional differences in RP and RT were observed ($P \leq .0001$). RP was used most commonly in the Midwest (75.07%) and High Plains (73.37%) regions, whereas RP was least used in the South Atlantic (59.04%) region. Similarly, RT was used most commonly in South Atlantic (40.96%) and New England (38.98%) regions and least commonly in the Midwest (24.93%) region. AS was used most in the New England (7.27%) and Midwest (6.8%) regions and least used in the High Plains (2.57%) and Mid-South (2.84%) regions.

Conclusions: Regional differences exist in the United States with regard to the definitive treatment of localized prostate cancer. The etiology for these regional differences is likely multifactorial.

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Sources of support: This work had no specific funding.

Conflicts of interest: Dr. Steven J. DiBiase is a member of the Speakers Bureau for Bayer Pharmaceuticals and a consultant for UpToDate.

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<https://doi.org/10.1016/j.adro.2019.01.004>

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Introduction

Newly diagnosed localized prostate cancer affects approximately 233,000 men in the United States each year. Prostate cancer accounted for 29,480 deaths in 2014.¹ It is the most commonly diagnosed and second most lethal cancer in men, trailing only lung cancer. Men have many treatment options for localized prostate cancer. The most commonly used treatments are surgery (radical prostatectomy [RP]), radiation therapy (RT; eg, external beam radiation therapy [EBRT], brachytherapy), and active surveillance (AS). Determining the right treatment option for a given patient is complicated and often depends on physician and patient preference. Early detection of prostate cancer has been linked to overtreatment and unnecessary morbidity.^{2–4} To minimize morbidity from aggressive treatment, watchful waiting and AS strategies are often used. These strategies work best for men with low-risk, localized prostate cancer and might be appropriate for men with intermediate disease.^{5,6}

Studies on the efficacy of specific treatment modalities are complex and often inconclusive. A recent study in the *New England Journal of Medicine* found no significant difference in mortality at 10-year follow-up among RP, EBRT, and AS.⁷

We sought to investigate whether there are regional differences in the management of localized prostate cancer, specifically with regard to surgical and radiation options. The literature on this subject is limited. We seek to update the study by Mettlin et al from 1997 in addition to analyzing regional differences in AS utilization.⁸ Our study does not aim to provide specific reasons for any observed regional differences, but we hope that these data will be hypothesis-generating and allow physicians, patients, and hospital administrators to guide their respective practice to maximize patient outcomes and better understand their practice in regard to their own geographic region.

Methods and Materials

Using the National Cancer Database (NCDB), we identified men who were diagnosed with localized prostate cancer in the United States between 2010 and 2014. Localized prostate cancer in this study was defined as non-metastatic prostate cancer that consisted of American Joint Commission on Cancer stages I through III.

The NCDB is a clinical oncology database sourced from hospital registry data that are collected in more than 1500 Commission on Cancer–accredited facilities. Comparisons of the NCDB with population-based registry data have demonstrated that the NCDB is representative

of cancer care at the community level in the United States. NCDB data are collected using a computerized, standard format that has been described elsewhere.⁹ The data represent >70% of newly diagnosed cancer cases in the United States and >34 million historical records.¹⁰ Hospital participation is voluntary, and hospital cancer committees or their equivalent oversee data collection and quality assurance. Although responsible for the collection and distribution of the data, the Commission on Cancer of the American College of Surgeons and the American Cancer Society are not responsible for the present analysis or our conclusions.

The United States was divided into 11 regions based on the American Cancer Society Divisions (Fig. 1). The first course of treatment was recorded as RT, RP, or AS. RT encompassed all forms of RT, including but not limited to EBRT, combination EBRT and brachytherapy, and brachytherapy as monotherapy. The RT subgroup consisted of patients receiving RT only, or RT plus androgen deprivation therapy (ADT), because radiation was the primary treatment modality. ADT was defined as medical or surgical therapy (orchiectomy), and RP was defined as a total prostatectomy (excised prostate, ejaculatory duct, and seminal vesicles) with and without lymph node dissection. The RP subgroup consisted of patients receiving either RP as a sole treatment or combined with RT or ADT; surgery was the primary, upfront treatment recommendation. Patients who received ADT only, no first course treatment, or another specified treatment were excluded from the study. Patients who received treatment after a period of AS were removed from the study. Subtotal prostatectomy or more extensive surgery, such as cystoprostatectomy, was classified as other treatment. Patients who received chemotherapy, biologic response modifiers, or experimental treatment also were classified as having received other treatment. Transurethral resection of the prostate was not considered cancer-directed treatment and thus was recorded as no treatment.

All data for study specific variables were summarized using descriptive statistics. Frequency tables were drawn up for nominal and ordinal data. A χ^2 test was used to assess the association between region and frequency of RT, RP, and AS. A 2-sided 5% significance level was used throughout the analyses. All analyses, summaries, and listings were performed using SAS software (version 9 or higher in a Windows environment).

Results

This study included 462,811 men with localized prostate cancer treated in the United States, of whom 63.46% underwent RP, 31.54% underwent RT, and 5.00% underwent AS. When comparing regional differences in RP versus RT, significant differences were

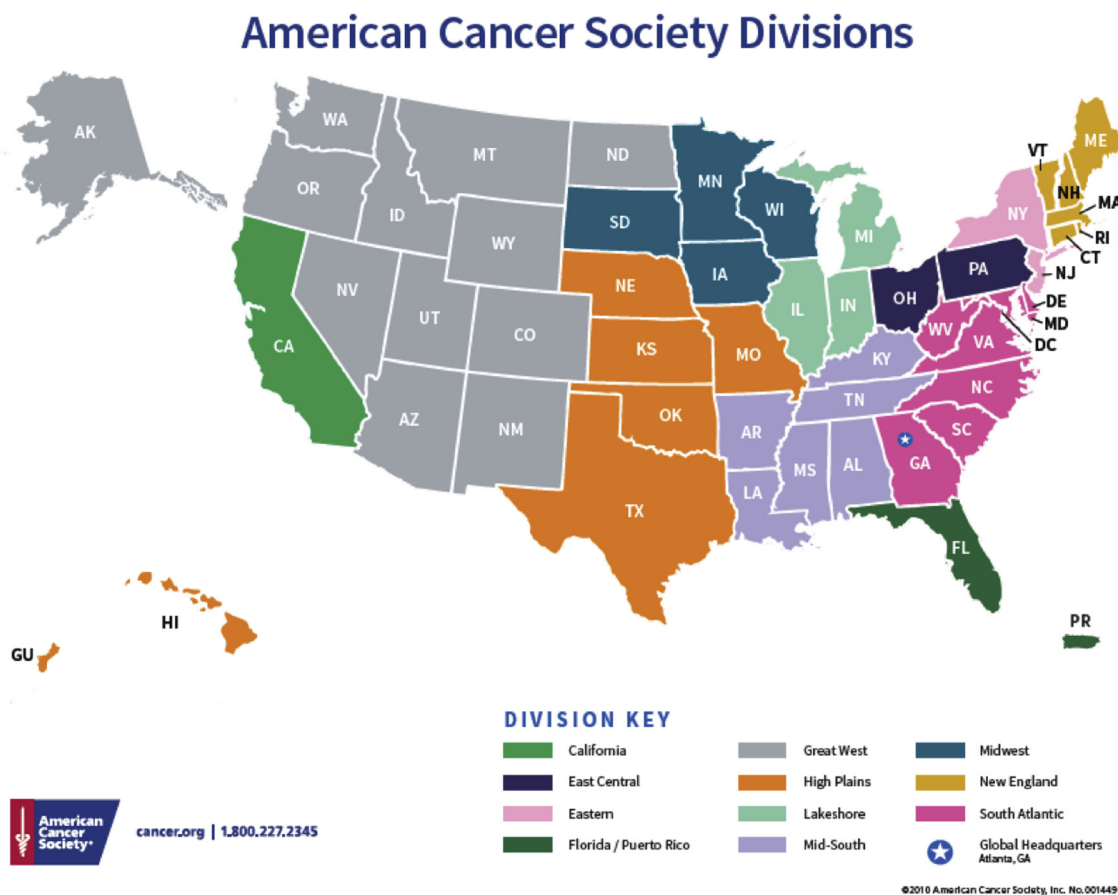


Fig. 1. American Cancer Society divisions map.

observed (Fig. 2). A χ^2 analysis of the data yielded a *P*-value of $< .0001$. RT was used most commonly in the South-Atlantic (40.96%), New England (38.98%), and California (36.39%) regions and least commonly in the Midwest (24.93%), High Plains (26.63%), and Great West (27.44%) regions. Similarly, RP utilization varied based on region ($P \leq .0001$). RP was used most commonly in the Midwest (75.07%) and High Plains (73.37%) regions, whereas RP was least used in the South Atlantic (59.04%) and New England (61.02%) regions.

When regions are more broadly grouped, there is a high rate of RP predominantly in the Central and Southern United States (ie, Midwest, High Plains, Great West, Florida, Mid-South, and Lakeshore; 71.65%) compared with the Eastern United States (ie, South Atlantic, New England, East Central, Eastern) and California (61.78%; $P \leq .0001$). Regions in Eastern United States and California use RT at a higher rate (38.22%) than the Central and Southern United States (28.35%; $P \leq .0001$).

There was also regional variation in AS utilization (Fig. 3). AS was employed most commonly in the New England (7.27%) and Midwest (6.8%) regions and used least in the High Plains (2.57%) and Mid-South (2.84%) regions.

Discussion

Men with localized prostate cancer have several options in their treatment. However, the best approach is controversial in light of the lack of randomized, phase 3 trials. As a result, treatment decisions vary based on multiple factors. In this paper, we examined the influence of location on the management of prostate cancer, and found significant differences throughout the United States in prostate cancer management. The Central and Southern regions of the United States employ more surgery and less radiation than the Northeast, Atlantic, and California regions.

These regional differences have been previously described in 1997 by Mettlin et al, who found that RT was used more commonly in the Northeast and Southeast regions of the United States compared with the rest of the United States.⁸ They also found that RP was used more commonly in the Mountain-Pacific, South, and Midwest regions compared with other regions.

Our study yielded similar results, with surgery still more commonly used in the Midwest, South, and Western regions, whereas RT is used $>38\%$ of the time in the Northeast and Southeast regions. Thus, the regional

PROSTATE CANCER TREATMENT BY REGION

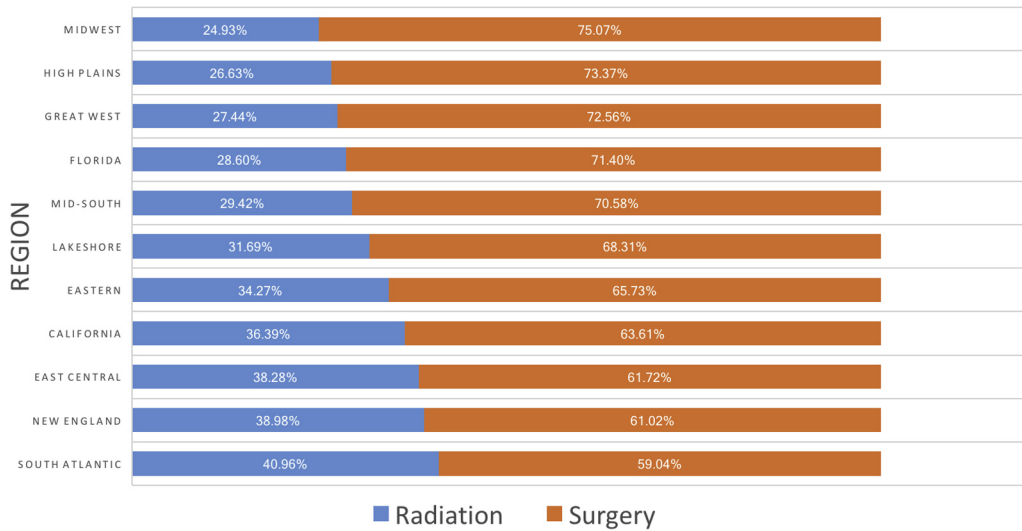


Fig. 2. Regional differences in radiation versus surgery for prostate cancer treatment.

patterns of prostate cancer management have largely stayed the same over the past 20 years. A notable exception is California, where radiation is used at rates similar to those on the East Coast of the United States. The reason behind these differences is likely multifactorial. Of note, the period between 2010 and 2014 does not highlight the greater use of AS seen in recent years.¹¹

Camarata et al found that EBRT utilization rates were increased in independent cancer centers compared with large multispecialty groups (37.00% vs 13.23%; $P < .001$).¹² Their findings are consistent with those of other studies that showed increased use of radiation in

free-standing radiation centers owned by non-radiation oncology physicians (most commonly urologists).^{13,14} This may be influenced by the fee-for-service model and associated financial motivations, as well as referring-physician treatment modality preference. Medicare reimbursements for RT are often more than twice that of surgery, which might financially influence urologists to recommend RT over surgery.¹⁵ There is much disagreement with regard to the value of these practices.^{16,17} Further studies are warranted to investigate the role independent cancer centers play in the regional differences in the management of localized prostate cancer.

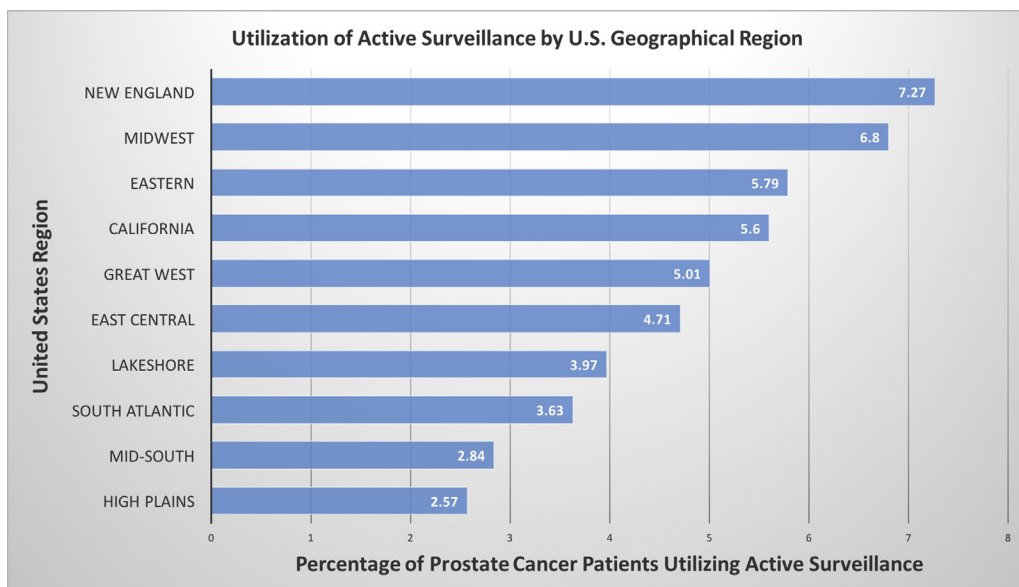


Fig. 3. Utilization of active surveillance by U.S. geographical region.

Another possible contributing factor to these regional differences is the density and availability of both urologists and radiation oncologists. For men with moderately differentiated, clinically localized cancers and a >10-year life expectancy, 93% of urologists chose RP as the preferred treatment option, but 72% of radiation oncologists believed surgery and EBRT were equivalent treatments.¹⁸ Thus, specialists are more likely to recommend the treatment approach that they themselves perform. Training patterns, such as with robotic surgery, may also influence treatment choices. One study suggested that robotic-assisted RP is used more in the Midwest than in other regions of the United States.¹⁹ Perhaps this adoption contributes to the high rate of prostate surgery in the Midwest.

Job availability and residency training density may also affect prostate cancer treatment. Significant regional imbalances of academic versus nonacademic radiation oncology jobs, regional job availability, and a surplus of radiation oncology trainees may exist in the Northeast.²⁰ There are also more National Cancer Institute–designated cancer centers in the Northeast and South Atlantic regions than other regions in the United States. One study found that the further patients live from a radiation center, the less likely they are to choose radiation for their prostate cancer treatment.²¹ Because there are more trainees and radiation oncology jobs in the Northeast, more patients live near a radiation center. The combination of all of these factors in the Northeast likely contributes to the regional differences in management as described.

For patients with a diagnosis of low- and sometimes intermediate-risk prostate cancer, AS has progressively been accepted as a viable means of treatment. The goal of AS is to limit the overtreatment of patients by differentiating between cancers with biological potential and strictly indolent cancers, which are ideally left untreated. In a prospective study of 993 men at a single health center, participants had an 85% survival rate with a median follow-up time of 6.4 years from the primary biopsy.²² The study concluded that AS is an achievable option with favorable-risk patients over a 15-year time period. Although there have been consistent demonstrations in the literature of the utility of AS, more research is needed with regard to biomarkers, imaging studies, and genetics that might predict the risk of cancer progression.²³

Regional differences in the utilization of AS for prostate cancer management have been previously described in the literature.²⁴ Patients in New England were found to be more likely to undergo AS than those in other regions for very low-risk prostate cancer diagnosed between 2004 and 2013. Our study finds similar results and demonstrates that the New England region continued to use AS more often than other regions between 2010 and 2014. The reasons for this are likely similar to those

previously described for RT, namely the increased proportion of academic centers in the Northeast.²⁰

Overall, there are likely many reasons that produce regional variations in the management of localized prostate cancer. There are still myths and a lack of knowledge about cancer worldwide, but recent awareness campaigns have overall improved patient education.²⁵ Patient preference and cultural differences are difficult to quantify, and there is a paucity of data with regard to these factors within the different regions of the United States. However, these differences might also play a factor in the differences described in our analysis.

Our study aimed to describe the regional utilization of common management strategies for prostate cancer. Limitations of our study include its retrospective nature, lack of differentiation by risk group, and lack of risk group differentiation by region. In addition, our study does not subcategorize different surgery and radiation modalities by region. The NCDB considers treatment after AS subsequent treatment, and not AS. Therefore, we were unable to account for men who received AS before treatment, which is a limitation of our study.

Despite these limitations, we believe that our results and analysis add to the limited body of literature on this subject and allow health care providers to tailor and refine their management either to be more in line with their region or to advance a certain treatment modality that might be lacking in their region. Future studies that are prospective and multivariant might be helpful in further elucidating the relationships described.

Conclusions

Regional differences exist in the United States with regard to the definitive treatment of localized prostate cancer. The etiology for these regional differences is likely multifactorial, involving physician and patient preference, access to radiation centers, density of urologists and radiation oncologists, and payment models. Additional research with regard to independent cancer centers, patient preferences, and regional cultural attitudes toward surgery and radiation would be helpful in further elucidating this relationship.

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