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The Influence Of Regional Health System Characteristics On The Management Of Glioblastoma Multiforme

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ABSTRACT

THE INFLUENCE OF REGIONAL HEALTH SYSTEM CHARACTERISTICS ON THE MANAGEMENT OF GLIOBLASTOMA MULTIFORME. Dhruv Khullar, Sanjay Aneja, James B. Yu. Department of Therapeutic Radiology, Yale University, School of Medicine, New Haven, CT.

Despite a known optimal treatment protocol for the management of glioblastoma multiforme (GBM), many patients fail to receive complete surgical resection or post-operative radiation therapy (PORT). The underlying reasons behind this disparity are unclear. We hypothesize that regional health system resources influence the surgical management and PORT in patients with GBM.

Surgical intervention, PORT receipt, and patient data for patients diagnosed with GBM from 2004 to 2008 were obtained from the NCI Surveillance, Epidemiology, and End Results (SEER) database and combined with the health system data from the Area Resource File. Health system characteristics studied included radiation oncologist density, neurosurgeon density, primary care provider (PCP) density, general radiation therapy (RT) and/or medical oncology (MO) equipped hospital density, and median household income. The geographic units of analysis were NCI-defined Health Service Areas (HSA) within the SEER registry. Four logistic models were constructed to test the effect of health system characteristics on surgical treatment choice and PORT receipt.

Of the 8,337 patients in our sample that were diagnosed with GBM, 71.45% received PORT. We found that younger, married patients in HSAs with higher median incomes were significantly more likely to receive both gross total resection ($p < .001$, $p < .001$, $p = 0.002$) and PORT ($p < .001$, $p < .001$, $p = .008$). For every $10,000 increase in the median income of a HSA, a patient's likelihood of receiving gross resection and PORT increased by 7% and 6.3%, respectively. The density of primary care providers and radiation oncology equipped hospitals were also significant predictors of PORT receipt ($p = .024$, $p = .002$). Patient race, radiation oncologist, and neurosurgeon densities were not associated with likelihood to receive PORT

Our findings suggest that regional variations in neuro-oncology services and income may have impact on GBM management. The presence of hospitals with oncology services within an HSA was more predictive of PORT receipt than the density of radiation oncologists and neurosurgeons themselves, suggesting that hospital-level infrastructure is needed to optimize care of GBM, independent of physician staffing levels. Policies aimed at narrowing disparities in treatment may need to focus on addressing regional variations in oncology resources.

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My sincere thanks also to Dr. Jack Hughes, who first inspired in me the desire to explore how the ways that we care for our patients are influenced profoundly by the habits we cultivate, the choices we make, and the health care system in which we practice.

Finally, thank you to my wonderful and supportive friends in New Haven and elsewhere, who have made the past five years some of the richest, most rewarding, and most memorable of my life.

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DISCLOSURE

Please note that a significant portion of the Methods and Results sections (including Figures and Tables) are taken from a recently published paper, on which I am an author. To a lesser extent, the Introduction and Discussion contain some material from this paper. The citation is as follows:

> *Aneja S, *Khullar D, Yu JB. The influence of regional health system characteristics on the surgical management and receipt of post operative radiation therapy for glioblastoma multiforme. *J Neurooncol.* 2013 May; 112(3):393-401.

INTRODUCTION

The Physician Workforce

Understanding the composition of the physician workforce and the organization of health systems is becoming increasingly important as the United States continues to reform its health care system in pursuit of higher quality, broader access, and greater efficiency. Though concerns about an inadequate physician supply have been noted for decades,[1] the passage of the Affordable Care Act (ACA)—and the subsequent influx of millions of Americans into the health care system—have brought these issues to the forefront of recent health policy debates.[2,3] By some estimates, the current physician shortage is expected to swell to 130,000 physicians by 2025, including a quadrupling of the specialist shortage.[4,5] While the ACA's insurance expansion may exacerbate the predicted physician shortage, population growth and aging are thought to be the primary drivers of increased health care utilization.[6] The recently established National Healthcare Workforce Commission is charged with monitoring the supply and distribution of physicians.

Already, low-income individuals in the United States report greater difficulty accessing health care than their counterparts in other industrialized countries.[7] The ACA's coverage expansion may help alleviate these difficulties, but it can only do so if there is an adequate physician supply to meet greater demand. Some have argued that greater dependence of mid-level providers offers a cost-effective avenue to fill the physician shortage, especially in primary care.[8,9]

Over the past decade, there has been a fifteen-fold increase in Medicare patients receiving care from nurse practitioners. Not surprisingly, states with less restrictive regulations have seen the greatest increase in the use of nurse practitioners as primary care providers.[10] Nurse practitioners and physician assistants may also have an increasingly important role to play in the delivery of cancer care, given the increasing complexity of oncologic care and projected increase in demand for oncology services.[11,12] But the ability of mid-level providers to address physician shortages is not without controversy, and physicians and mid-level providers have been found to disagree significantly on their respective roles in the delivery of medical care.[13]

Geographic Maldistribution of Physicians

While some are concerned about an absolute shortage of physicians, others contend that a geographic maldistribution of providers is an equally important threat to access and quality.[14,15] Recent analyses suggest that states with more physicians tend to have better health care access and higher quality.[16] This may be especially true for primary care physicians. The primary care physician supply has been associated with a host of better health outcomes including improvements in all-cause mortality, cancer, heart disease, stroke, infant mortality, and life expectancy.[17,18]

Simply increasing the overall supply of physicians may not address the regional differences in physician supply, as physicians tend to settle in areas that already have a relatively high density of providers. One study found that while there was a 50% increase in physicians per-capita from 1979 to 1999, for every four physicians that settled in a high-supply region, only one settled in a low-supply region.[18,19] Another study found that while the number of cardiologists has increased modestly since the 1990s, a significant maldistribution of the workforce persists, with 60% of the elderly having access to less than 40% of cardiologists. Rural and low socioeconomically disadvantaged areas are more likely to have lower concentrations of cardiologists.[20]

This geographic maldistribution may be even more pronounced for smaller specialties, with rural areas experiencing the lowest physician-to-population ratios.[21] For example, while the radiation oncology workforce increased 24% from 1995 to 2007, there is considerable variability in the density of providers across the country. Areas with higher education, higher income, and higher minority populations seem to have higher radiation oncologist-to-population ratios.[22] Ensuring patients have adequate access to the services they need in the coming years will require policies aimed not only at increasing the absolute number of physicians, but also addressing how those physicians are distributed.

Physician Density and Health Outcomes

There is growing evidence that health system characteristics like the distribution of providers can influence the type and quality of medical care delivered. A recent analysis found that as compared to Medicare beneficiaries living in regions with low primary care physician density, those in higher density areas had lower mortality rates and fewer hospitalizations.[23] Medicare patients in poor or fair health are almost twice as likely to have a preventable hospitalization if they live in an area with a primary care shortage.[24]

These effects may be especially pronounced for patients with chronic illnesses who require frequent contact with the health system to appropriately manage their disease. One recent study found that heart failure patients residing in rural, low socioeconomic, and low physician density regions are less likely to receive early follow-up after being discharged from the hospital, significantly increasing their risk for readmission.[25] Another study focused on hospitalizations for inflammatory bowel disease (IBD). It found that while the rate of IBD hospitalizations was similar in high physician density and low physician density counties, patients in high density counties presented to the hospital with less complicated disease and ultimately had lower hospitalization charges.[26]

Health System Characteristics and Oncologic Care

The influence of regional health systems and physician workforce on cancer care specifically is also increasingly being recognized. Physician density has been shown to influence health outcomes in a variety of diseases,[27,28] and evidence suggests that the density of primary care physicians may be particularly important for reducing cancer mortality rates.[29] Significant and persistent geographic maldistributions of oncologic specialists and health resources have also been associated with variations in treatment patterns, as well as clinical outcomes, and highlight a potential driver of cancer-related disparities.[22,30]

The effect of physician supply on cancer care is often nuanced and complex. For example, one recent study found that the presence of at least one urologist per county is associated with reduced mortality for urologic cancers. However, a density greater than two urologists per 100,000 people yields no additional mortality benefit.[31] Higher densities of gastroenterologists reduced delays in diagnosis of gastric cancer in rural areas, but additional gastroenterologists had no effect in urban areas, where the density of physicians is already relatively high.[32] Similarly, higher gastroenterologist density is associated with a 14-17% reduction in late-stage colorectal cancer in non-metropolitan counties.[33] Women living in areas with more mammography facilities and an adequate supply of primary care providers are more likely to adhere to mammography screening guidelines.[34]

Evidence from other countries also supports the hypothesis that local health resources and physician density have an important impact on cancer screening and treatment. In Canada for example, women with breast cancer who reside in areas with higher OB/GYN and primary care densities have higher survival rates at 5 years.[35] In Germany, increases in physician supply have been associated with small reductions in avoidable deaths for cancers of the breast, colon, rectum, and anus.[36] Researchers in France found that women living in areas with low practitioner density were at higher risk for delayed cervical cancer screening.[37,38]

In the United States, the recent health reform legislation has placed a new focus on assessing the adequacy of the supply and geographic distribution of the physician workforce.[39] At a time when the health care system is in flux, a deeper understanding of how the distribution of specialists and oncology centers influences cancer treatment may be helpful for developing policies that promote better patient outcomes. Our study investigates the influence of regional health system resources on the treatment of a particularly aggressive type of cancer, glioblastoma multiforme (GBM), by examining its surgical management and the receipt of post-operative radiation therapy (PORT) across the United States.

Disparities in Management of Glioblastoma Multiforme

GBM is the most common brain tumor in adults and continues to carry a very poor prognosis with a median survival of approximately one year.[40] It accounts for approximately 25% of primary CNS tumors in adults, and the annual incidence is 5 per 100,000.[41] Risk factors include male gender, age greater than 50, history of receiving radiotherapy, having a low-grade brain tumor, genetic disorders such as neurofibromatosis, and Caucasian, Asian, or Hispanic ethnicity.[42] Patients often present with new onset headaches or seizures, progressive cognitive dysfunction, behavioral and personality changes, and neurological deficits depending on location of the tumor.

GBM offer appears as a ring-enhancing lesion when viewed on MRI, but definitive diagnosis requires biopsy and pathologic confirmation. A number of diagnostic and prognostic molecular tests are routinely performed, including testing for chromosome

1p and 19q deletions,[43] MGMT promoter methylation,[44] and IDH1/IDH2 enzyme mutations.[45]

While GBM carries a poor prognosis, several factors are associated with improved survival including lower tumor grade, younger age, and better Karnofsky performance status.[40] Patients with frontal lobe tumors have longer median survival after surgery compared to those with temporal or parietal lobe tumors.[46] The current standard of treatment for GBM includes maximal surgical resection followed by post-operative radiation therapy (PORT) in combination with chemotherapy.[47] Some authors have found the extent of surgical resection to be the most important prognostic factor in patients diagnosed with GBM.[48] Gross total resection—removal of all visibly abnormal tissue seen on MRI or intraoperatively—should be attempted when possible, and tumor biopsy or partial resection should be considered only when total resection is determined to be unsafe or unfeasible.[48,49]

Partial resection seems to improve outcomes as compared to biopsy only, suggesting a survival benefit of tumor debulking. One recent study found significant survival benefit with subtotal resections as low as 78% of tumor.[50] Regardless of the extent of initial resection, gross total resection should be attempted on recurrence, as it has been found to overcome the effect of initial subtotal resection and maximize survival.[51]

Because microscopic residual disease remains even after removal of the visible tumor, surgical resection should be followed by PORT administration. Randomized controlled trials have found a doubling of survival in some patients who receive PORT.[52,53] Regardless of extent of tumor resection, patients receiving adequate doses of PORT have longer median survival,[54] and radiotherapy has been shown to improve survival in both young and elderly GBM patients.[55] This regimen may increase functional status and survival even in patients with relatively low Karnofsky Performance Scores.[56]

More recently, studies have shown that temozolamide administered in conjunction with PORT can improve survival.[57] Authors have found an increase in median survival of 2.5 months with limited adverse effects in patients receiving temozolamide in addition to radiotherapy, as compared to radiotherapy alone. Recent trials continue to provide further support for use of temozolamide to improve overall and progression free survival.[58] While the cost of adjuvant temozolamide is substantial, several authors have concluded that it is a cost-effective addition to GBM management, especially if the generic drug is used, with quality-adjusted life year gains comparable to other first-line chemotherapeutic agents.[59,60] However, others argue that the addition of temozolamide in resource-poor health settings is not cost-effective, and should be used preferentially in subgroups with more favorable prognostic factors.[61]

Regional health system resources have been associated with variations in outcomes in a number of cancers, but these factors have not been well-described in the treatment of GBM. Despite an established optimal treatment protocol, some patients with GBM fail to receive complete surgical resection or PORT, highlighting a concerning gap in treatment.[40] The underlying reasons behind the disparity in treatment are poorly understood, but are particularly troubling given the high mortality rate associated with GBM. In the United States, the density of neurosurgeons and radiation oncologist specialists varies significantly by county.[22] Workforce discrepancies persist when examining density of hospitals providing oncologic services, thus leaving segments of the population without access to the specialized care they need. These variations may contribute to disparities in the treatment that GBM patients receive and ultimately their survival outcomes.

SPECIFIC AIMS

1. To understand whether patient and health system characteristics are associated with variations in the surgical management of patients with GBM.
2. To understand whether patient and health system characteristics are associated with receipt of post-operative radiation therapy for patients with GBM.
3. To examine regional variations in the density of neuro-oncologic providers and hospitals (i.e., neurosurgeons, radiation oncologists, general oncologists) across the United States

METHODS

Data Sources and Study Sample

There were two primary data sources utilized in this study. Clinical data was derived from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) public-use database. The SEER dataset began in 1973 and collects information on incident cancer cases, now covering approximately 26% of the United States from 17 cancer registries.[22,62] The dataset provides clinical information including patient age, gender, race, marital status, histology, primary tumor site, morphology, stage at diagnosis, initial treatment, and overall survival.

The study sample included patients within the SEER dataset aged 18 years or older diagnosed with GBM (International Classification of Diseases for Oncology, Version 3 histology codes 9440–9442) between the years 2004 and 2008. Patient data of interest included patient age, race and marital status. Clinical data studied included type of surgical intervention and whether the patient received post-operative external-beam radiation therapy.

Health system data was obtained from the 2007 edition of the Area Resource File (ARF). Published by the Health Resources and Services Administration of the United States Department of Health and Human Services, the ARF is a collection of data from over 50 sources, including the American Medical Association, American Hospitalization Association, US Census, and National Center for US Health Statistics.[63] The ARF aggregates information concerning the health care professionals, health care facilities, and population for each county in the United States. Health system characteristics studied included number of population, radiation oncologists, neurosurgeons, primary care physicians, radiation therapy-equipped hospitals, general oncology equipped hospitals, and median household income within a county from 2004 to 2008.

Construction of Variables

All statistical analyses were carried out with the help of Sanjay Aneja, MD. The geographic units of analysis were the 154 Health Service Areas (HSAs) within the SEER dataset as defined by the National Center for Health Statistics and National Cancer Institute. HSAs are defined as a single county or group of contiguous counties that remain self-contained with respect to hospital care. HSAs were chosen as the unit of analysis because they best represent geographic access to healthcare within a region. County level data from the ARF was aggregated to HSAs using simple summation for physician and population variables and population weighted sums descriptive variables. Physician and hospital densities were calculated at 5-year population averages per 100,000 residents. To isolate patients who were candidates for curative treatment and to prevent immortal time bias, patients who did not receive any surgical intervention or those who died within 6 months of diagnosis were excluded from the analysis.[64] Additionally, patients who received radiation other than external-beam radiation therapy were excluded from the analysis.

Statistical Analysis

To visually evaluate the relative distribution of neuro-oncologic resources across the United States, physician densities and hospital densities were mapped using to corresponding HSAs using the geographical information system ArcGIS Version 9.2 (Environmental Systems Research Institute, Inc., Redlands, CA).

A total of four logistic models were constructed to test the effect of health system characteristics on surgical treatment choice and receipt of post-operative radiation therapy (PORT). Three logistic models were built to test the influence of regional health care systems on whether patients underwent gross total resection, partial resection, or only biopsy. Because we assumed that radiation therapy services were unlikely to be related to initial surgical treatment choice, density of radiation oncologists and radiation therapy equipped hospitals were excluded from the surgery logistic models. To test the factors associated with the receipt of PORT a fourth logistic model was build, which included radiation oncologist and radiation therapy equipped hospital density. Statistical significance was determined at $p<.05$. Statistical analysis was conducted using Stata Version 9.2 (Stata, College Station, TX).

RESULTS

In total, 8,337 patients within the SEER dataset were diagnosed with GBM from 2004 to 2008. Of these, 2,346 (28.2%) were excluded because they received only radiation therapy (1,207 patients) or no curative treatment (1,139 patients). Our final study cohort included 5,991 patients with a mean age of 61 years ranging from ages 18 to 95.1 years. 68.1% of the study sample was married and 90.6% was white.

Patients were more likely to receive gross total resection and PORT (38.6%) than any other treatment regimen. However, a substantial proportion of patients received partial resection and PORT (29.8%) or only biopsy and PORT (15.5%). A smaller number of patients received gross resection (7.7%), partial resection (8.2%), or biopsy only (4.8%) without PORT.

We found that the density of neurosurgical, radiation therapy, and general oncology services varied geographically among different HSAs within the SEER registry. Moreover, we found a geographic maldistribution of both specialists and hospitals across all HSAs within the United States (Figure 1 and 2). Among the HSAs studied we found significant variability in the density of radiation oncology hospitals (median = 2.52 per 100,000 residents, range = 0 to 4.09), general oncology hospitals (median = 0.537 per 100,000 residents, range = 0 to 14.3), neurosurgeons (median = 1.7 per 100,000 residents, range = 0 to 5.13), and radiation oncology specialists (median = 1.42 per 100,000 residents, range = 0 to 3.55). The median household income of HSAs analyzed was found to be $56,800 with a range of $24,770 to $90,800.

Predictors of gross resection are listed in Table 1. Younger, married patients who lived in HSAs with higher median incomes were significantly more likely to receive gross total resection ($p < .001$, $p < .001$, $p = 0.002$). For every $10,000 increase in the median income of a HSA, a patient's likelihood of receiving gross resection increased by 7%. Importantly, patient race, density of neurosurgeons, and density of oncology departments were not associated with complete resection.

Table 1: Predictors of Total Gross Resection

Predictors of Total Gross Resection	**Odds Ratio**	**Error**	**p**	**95% Confidence Interval**	
Neurosurgeon Density	1.00	0.04	0.911	0.91	1.08
White Race	1.08	0.10	0.430	0.90	1.30
Married	1.91	0.11	<0.001	1.71	2.13
Age	0.95	0.01	<0.001	0.94	0.95
Median Household Income of HSA	1.06	0.01	0.028	1.01	1.12
Medical Oncology Equipped Hospital Density	1.07	0.04	0.580	1.00	1.16

Figure 1: Geographic Distribution of Neurosurgeons and Radiation Oncologists Across the United States.

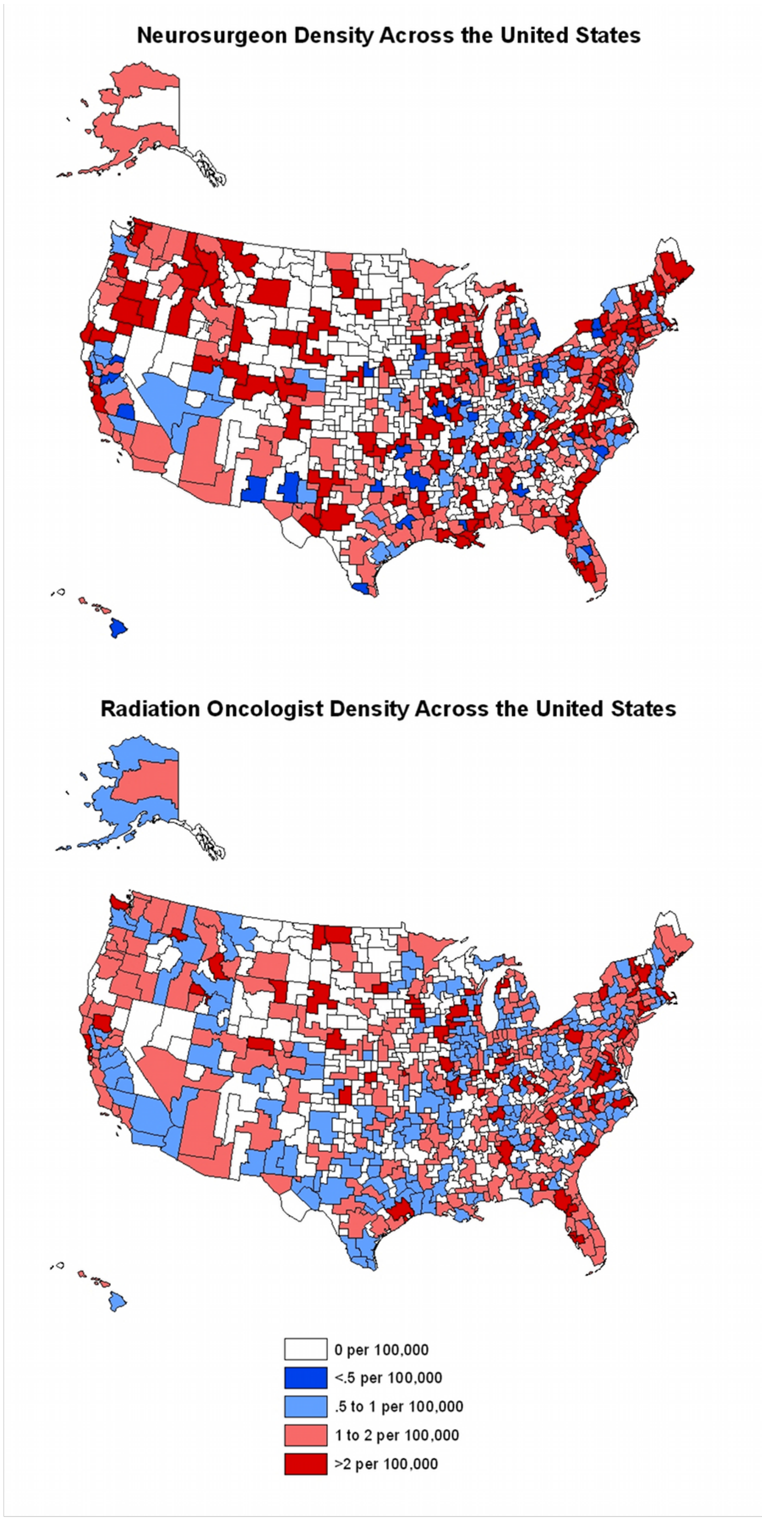
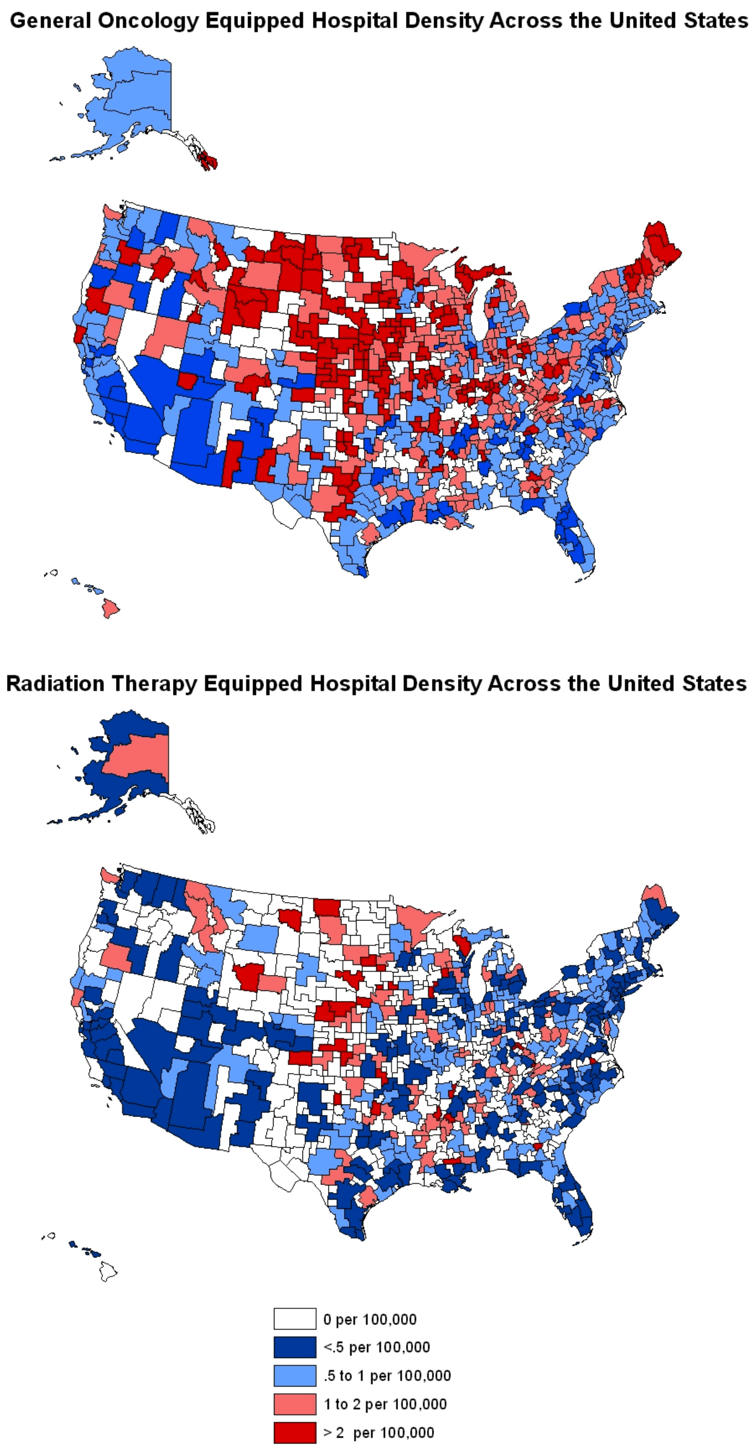


Figure 2: Geographic Distribution of General Oncology and Radiation Therapy Equipped Hospitals Across the United States



Unmarried patients from HSAs with lower median incomes were associated with receiving biopsy only (p = .004, p < .001). As the median income of a patient's HSA decreases by $10,000, a patient becomes 15% more likely to receive biopsy only for treatment of GBM. Unmarried patients were 18% more likely to receive biopsy only. Patient age, race, density of neurosurgeons, and density of oncology departments were not associated with likelihood of biopsy. These results are presented in Table 2. Partial tumor resection was not associated with any patient, population, or health system characteristics analyzed in our model (Table 3).

Table 2: Predictors of Biopsy Only

Predictors of Biopsy Only	Odds Ratio	Error	p	95% Confidence Interval	
Neurosurgeon Density	1.03	0.04	0.352	0.96	1.11
White Race	0.94	0.10	0.607	0.76	1.17
Married	0.82	0.06	0.004	0.72	0.94
Age	1.00	0.01	0.147	0.99	1.01
Median Household Income of HSA	0.85	0.01	<0.001	0.80	0.89
Medical Oncology Equipped Hospital Density	0.94	0.04	0.148	0.86	1.02

Table 3: Predictors of Partial Resection

Predictors of Partial Resection	Odds Ratio	Error	p	95% Confidence Interval	
Neurosurgeon Density	1.00	0.03	0.991	0.94	1.06
White Race	0.87	0.08	0.141	0.73	1.05
Married	1.01	0.06	0.921	0.89	1.13
Age	1.00	0.01	0.257	0.99	1.01
Median Household	1.04	0.01	0.113	0.99	1.09

Income of HSA					
Medical Oncology Equipped Hospital Density	1.02	0.04	0.562	0.95	1.09

Overall, of the 8,337 patients diagnosed with GBM analyzed in our initial sample, 71.45% received PORT. The predictors of PORT receipt are listed in Table 4. As with extent of surgical resection, patient race was not associated with PORT receipt, but patient age and marital status were predictors of PORT receipt. Younger, married patients were more likely to receive PORT after surgery ($p < .001$, $p < .001$). Once again, the relative affluence of an HSA was significantly associated with a patient's likelihood of receiving treatment ($p = .008$). Every $10,000 increase in HSA median income increases the likelihood of PORT receipt by 6.3%.

Table 4: Predictors of PORT Receipt

Predictors of PORT Receipt	**Odds Ratio**	**Error**	**p**	**95 % Confidence Interval**	
Radiation Oncologist Density	1.07	0.07	0.258	0.95	1.22
Primary Care Physician Density	1.01	0.01	0.024	1.00	1.01
Neurosurgeon Density	1.00	0.04	0.911	0.91	1.08
White Race	1.08	0.10	0.426	0.90	1.30
Married	1.91	0.11	<.001	1.71	2.13
Radiation Oncology Equipped Hospital Density	1.43	0.14	0.002	1.18	1.74
Age	0.95	0.01	<.001	0.94	0.95
Median Household Income of HSA	1.06	0.01	0.028	1.00	1.12
Medical Oncology Equipped Hospital Density	1.07	0.04	0.058	1.00	1.16

There were also a number of health system factors associated with PORT receipt. The density of primary care providers (PCPs) and density of radiation oncology equipped hospitals were significant predictors of PORT receipt ($p = .024$, $p = .002$). Importantly, while the density of oncology-equipped hospitals predicts PORT receipt, the density of individual radiation oncologists and neurosurgeons were not associated with likelihood of receiving PORT. Overall, marital status and density of radiation oncology equipped hospital were the strongest predictors of PORT receipt (OR = 1.91, OR = 1.43).

DISCUSSION

Recent evidence has shown improvement in the outcomes of patients diagnosed with GBM. However, this improvement is seen only in patients who receive the recommended multidisciplinary treatment.[65] Our findings confirm a geographic maldistribution of radiation therapy and general oncology services that leaves significant portions of the population without ready access to radiation therapy.[22] We found that patient age, marital status, and median income of HSA are significant predictors of surgical resection and PORT receipt. The density of radiation oncology departments was also a predictor of PORT receipt. Our findings suggest that hospital infrastructure may be more closely associated with variations in GBM management than is physician supply. Regional variations in socioeconomic status are also associated with discrepancies in GBM treatment.

Extent of Surgical Resection

Some authors have found the extent of surgical resection to be the most important prognostic factor of GBM mortality. Both overall and event-free survival rates are substantially higher in patients who receive total tumor resection versus those who receive non-total resection.[48] A number of tumor characteristics including size, location, stage, and histology influence a surgeon's ability to achieve complete tumor resection.[49,66]

Given that the extent of tumor removal is a strong predictor of survival, maximal resection should be attempted whenever possible, and tumor biopsy or partial resection should be considered only when total resection is determined to be unsafe or unfeasible.[48,49] Our study corroborates previous findings that patient age and marital status predict likelihood of gross resection.[67] Furthermore, we found that every $10,000 increase in HSA median household income increases a patient's chances of achieving gross resection by 7%.

One possible reason for the socioeconomic disparity of patients undergoing gross total resection may be that those living in HSAs with higher median incomes have better access to hospital resources and improved coordination of care. Research has long demonstrated an association between low SES, limited access to health care services, and poorer health outcomes.[68-70] Low SES patients are more likely to use acute hospital care and less likely to use primary care services for a number of reasons, including perceiving hospital care as higher quality, more accessible, and less expensive.[71] Disparities in access may result from provider behavior as well. A recent study found that even in the absence of significant economic incentives, office staff are more likely to schedule high SES patients for an appointment, and that patients presenting themselves as high SES have preferential access to primary care services.[72]

Another potential explanation for the SES disparity we found is that individuals living in HSAs with higher median incomes present earlier in the disease course, and thus have smaller, more resectable tumors. Once again, this explanation is supported by research in other types of cancer. Recent studies examining patients with breast, prostate, colorectal, and testicular cancer suggest that low SES patients are diagnosed at a later stage and may receive a less aggressive treatment course.[73-75] Low SES prostate and breast cancer patients tend to have higher incidence, and worse mortality and survival rates than their more affluent counterparts.[76,77] Another study found that low SES was significantly associated with advanced tumor stage and reduced likelihood to pursue curative treatment, even when insurance coverage and access to health care were identical across groups.[78] Other work has found that lower patient education level is strongly associated with higher cancer death rates. For example, black men with fewer than 12 years of schooling had prostate cancer death rates more than twice that of black men with more schooling.[79]

Interestingly, in our study neither the density of neurosurgeons, nor the density of general oncology equipped hospitals was associated with likelihood of total resection. This suggests other factors associated with socioeconomic status may play a larger role in extent of surgical resection than number of physicians and hospitals. For example, it may be that surgeons in higher SES areas are more determined to obtain full resection, or patients from those areas are more ardent about pursuing one. There is some evidence to suggest that black and white patients are treated by different subgroups of physicians,[80] and that physicians may communicate differently with different subsets of patients.[81] Furthermore, differences in the hospitals in which minorities receive their care may contribute to the type and quality of treatment they receive, and ultimately result in poorer health outcomes. For example, minorities are more likely to undergo coronary artery bypass graft (CABG) surgeries in low-volume centers and performed by surgeons with higher risk-adjusted mortality rates.[82]

It is also possible that patients from lower SES areas have more comorbidities, and thus are less likely to pursue or be eligible for aggressive treatment. Evidence suggests that elderly GBM patients with more comorbidities are significantly less likely than their healthier counterparts to receive radiotherapy or chemotherapy.[83] More generally, low SES patients diagnosed with breast, lung, and colorectal cancer are more likely than high SES patients to have at least one other chronic condition.[84,85] One recent study found that low SES patients had a 50% increased risk of serious comorbidity—such as cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, or diabetes mellitus—than high SES patients, which partly explains disparities in one-year survival rates.[86]

The burden of comorbid disease in cancer patients may be increasing because of an aging and increasingly obese population. In a recent study of colorectal cancer patients, rates of comorbidity increased from 47% to 62% from 1995 to 2010, and multiple comorbidity rates from 20% to 37%, with hypertension and cardiovascular disease being the most prevalent. [84] These findings underscore the growing importance of optimal management of cancer patients with multiple comorbid conditions, especially for low SES patient populations.

As compared to biopsy only, partial resection seems to improve outcomes, suggesting a survival benefit of tumor debulking.[48] We found that partial tumor resection was not associated with any predictors in our model, suggesting that other factors such as tumor characteristics play a more important role in limited resection than do social and health system factors. As compared with complete resections, limited resections may be relatively unplanned occurrences influenced largely by intraoperative events or findings.

Factors Predicting PORT Receipt

Surgical resection should ideally be followed by PORT administration, as some randomized controlled trials have found substantial survival benefits in patients who receive PORT without significant adverse effects or reductions in quality of life or cognition.[52,53] Recently, survival rates have been found to improve further with the administration of concurrent temozolomide, though some trials have found higher risk of cognitive deterioration.[57,87]

Our study corroborates previous findings that PORT administration does not take place in a significant proportion of GBM patients,[88,89] with increasing patient age and unmarried status being associated with a lower likelihood of PORT. Other recent analyses have found that younger GBM patients (age < 70 years) have seen greater improvements in overall survival, potentially because of this disparity in PORT receipt.[90] As such, increased attention to and counseling for older, unmarried individuals may be warranted.

Unique to our study is the finding that the median household income of a patient's HSA significantly influences the likelihood of PORT receipt. We found that the administration of PORT follows a similar trend to surgical resection in that every $10,000 increase in HSA median income increases a patient's likelihood of receiving PORT by approximately 6%.

The association of lower income and worse health outcomes is well documented in a number of oncologic and non-oncologic diseases,[74,91-94] and new standards of care seem to disseminate more rapidly in high SES areas. For example, a recent analysis found that the examination of 12 or more lymph nodes in patients with colon cancer—a new standard of care—is more likely in high SES patients.[92] Patients in the highest SES quintile had a 30% increased odds of 12-node dissection as compared to patients in the lowest quintile. Similar results can be found in other areas. Men with testicular germ cell tumors living in low SES regions are more likely to present with advanced disease and have higher rates of mortality.[74] Patients from poorer areas are less likely to receive chemotherapy for melanoma than their more affluent counterparts.[91] However, the association of SES and management is a new finding with respect to patients with GBM.

The Complex Role of Provider Density

Our findings indicate that it may not be the density of individual radiation oncologists, but rather the prevalence of radiation oncology centers that influences PORT receipt, suggesting a dominant role of hospital-level infrastructure over individual providers for addressing disparities in GBM management. While the prevalence of specialists such radiation oncologists and neurosurgeons was not associated with PORT receipt, the density of PCPs was. The reason for this effect is unclear. It may be that PCP density is a proxy for a robust health system and effective coordination of care. Indeed, prior research suggest a number of salutary effects of health systems with strong primary care foundations, including lower health care costs, fewer hospital days, and better continuity of care.[18] Our finding further substantiates the importance of a region's health infrastructure as a significant predictor of PORT receipt in patients with GBM.

As we continue to search for ways to improve treatment of patients with GBM and other cancers, we would do well to keep in mind the influence of PCPs on early detection and comprehensive management. The ACA's emphasis on incentivizing integrated health care delivery systems may prove helpful in addressing some of the disparities stemming from fragmented care. The recent formation of hundreds of Accountable Care Organizations (ACOs)—provider networks responsible for the care of an attributed population of patients—may increase care coordination and improve timely diagnosis and treatment of cancers including GBM. Initial results from the evaluation of Medicare's Pioneer ACOs have been mixed, but some organizations have seen significant quality and efficiency improvements.[95]

Similarly, increasing interest in primary care-led organizations like Patient-Centered Medical Homes (PCMHs) with value-based reimbursement systems may help improve access and care coordination. More recently, Oncology PMCHs (OPCMHs) have been proposed as a model to integrate care, emphasize accountability, and enhance communication among providers and cancer patients.[96] In 2013, AETNA launched the first OPCMH in Pennsylvania, where patients can receive oncologic and non-oncologic care, in an effort to reduce cancer-related complications, emergency room visits, and hospital readmissions.[97] The efficacy of these health care delivery models for improving cancer management should continue to be evaluated in the coming years.

Patient Race and Management of GBM

Patient race has been associated with variations in care and outcomes in a variety of cancers.[98-101] However, in our study, race was not associated with variations in surgical management or receipt of radiation therapy for patients with GBM. In this sense, the management of GBM may be a model for other cancers, particularly those in which race-based disparity in treatment has been shown.[102-104]

However, this encouraging finding may be related to the relatively grave nature of GBM, and it is important to recognize the significant historical and pathophysiological differences between GBM and other malignancies. For example, while many breast and prostate cancer patients receive treatment in smaller free-standing centers, almost all GBM patients receive care in large academic centers. Furthermore, there is less controversy with regard to optimal screening and management of GBM patients as compared to other cancers. Lastly, the natural history of GBM predicts uniformly poor survival, while greater prognostic variation exists in other types of cancer.

Limitations

Our study has several limitations. Because the SEER dataset comprises only 26% of the US population, we must be cautious about generalizing findings to the country as a whole. That said, the SEER dataset has a relatively diverse geographic representation of health systems across the United States and includes registries from both rural and urban regions in many states. Another limitation of the SEER dataset is that it does not provide specific information regarding radiation therapy technique, dosage, and volume. However, this likely has a greater effect on survival analysis than on receipt of radiation therapy, the main variable assessed in this study. Finally, recent evidence has found the SEER dataset to underestimate the receipt of radiation therapy following breast-conserving surgery.[105] There has, however, been no similar evidence to suggest under-ascertainment for PORT in the setting of GBM.

The ARF also has several limitations that should be noted. First, the physician location data from the ARF is aggregated from the American Medical Association (AMA) Physician Masterfile. Because the AMA Masterfile does not account for physicians with multiple practices in different regions, it is possible that we overestimate the geographic clustering of radiation oncologists and neurosurgeons. However, while these specialists may practice in multiple locations, it is likely that their practices fall within the same HSA. Second, the ARF does not contain information regarding freestanding radiation therapy centers within different health systems. Nonetheless, our analysis suggests a relative maldistribution of radiation therapy services across the United States.

Finally, our study does not examine other barriers to care such as lack of health insurance and whether radiation oncology centers accept Medicaid payment for their services. Evidence suggests that, depending on the specialty, 30-50% of office-based physicians do not accept Medicaid, and that often, waiting times for Medicaid patients are significantly longer than for the privately insured.[106,107] These unexamined factors may also contribute to the disparities highlighted in this paper, and will be important to examine as states selectively expand Medicaid during implementation of the ACA.

CONCLUSION

In conclusion, meaningful discrepancies exist for GBM patients with regard to receipt of two important predictors of survival: gross resection and PORT. Our findings confirm that patient factors such as age and marital status influence a patient's likelihood of receiving full surgical resection and PORT. Furthermore, our findings suggest that a geographic maldistribution of oncology services and SES discrepancies in HSAs may have serious clinical implications for patients with GBM. Thus, policies aimed at narrowing disparities in treatment may need to focus on improving coordination of care and addressing gaps in oncology department density. Further studies are warranted to better understand the influence of health system resources on the extent of surgical resection and PORT receipt for GBM.

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