Trends in the utilization of radiotherapy for spinal meningiomas: insights from the 2004–2015 National Cancer Database

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OBJECTIVE Recent studies have reported on the utility of radiosurgery for local control and symptom relief in spinal meningioma. The authors sought to evaluate national utilization trends in radiotherapy (including radiosurgery), investigate possible factors associated with its use in patients with spinal meningioma, and its impact on survival for atypical tumors.

METHODS Using the ICD-O-3 topographical codes C70.1, C72.0, and C72.1 and histological codes 9530–9535 and 9537–9539, the authors queried the National Cancer Database for patients in whom spinal meningioma had been diagnosed between 2004 and 2015. Patients who had undergone radiation in addition to surgery and those who had received radiation as the only treatment were analyzed for factors associated with each treatment.

RESULTS From among 10,458 patients with spinal meningioma in the database, the authors found a total of 268 patients who had received any type of radiation. The patients were divided into two main groups for the analysis of radiation alone (137 [51.1%]) and radiation plus surgery (131 [48.9%]). An age > 69 years ($p < 0.001$), male sex ($p = 0.03$), and tumor size 5 to < 6 cm ($p < 0.001$) were found to be associated with significantly higher odds of receiving radiation alone, whereas a Charlson-Deyo Comorbidity Index ≥ 2 ($p = 0.01$) was associated with significantly lower odds of receiving radiation alone. Moreover, a larger tumor size (2 to < 3 cm, $p = 0.01$; 3 to < 4 cm, $p < 0.001$; 4 to < 5 cm, $p < 0.001$; 5 to < 6 cm, $p < 0.001$; and ≥ 6 cm, $p < 0.001$; reference = 1 to < 2 cm), as well as borderline ($p < 0.001$) and malignant ($p < 0.001$) tumors were found to be associated with increased odds of undergoing radiation in addition to surgery. Receiving adjuvant radiation conferred a significant reduction in overall mortality among patients with borderline or malignant spinal meningiomas (HR 2.12, 95% CI 1.02–4.1, $p = 0.02$).

CONCLUSIONS The current analysis of cases from a national cancer database revealed a small increase in the use of radiation for the management of spinal meningioma without a significant increase in overall survival. Larger tumor size and borderline or malignant behavior were found to be associated with increased radiation use. Data in the present analysis failed to show an overall survival benefit in utilizing adjuvant radiation for atypical tumors.

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KEYWORDS meningioma; radiotherapy; radiosurgery; national cancer database; trends; survival; spine tumor; spine neoplasms; Gamma Knife; adjuvant radiation

MENINGIOMAS are one of the most frequently encountered tumor types in the spinal cord, accounting for 20%–25% of all spine tumors.² Approximately 5%–14% of spinal meningiomas are extradural, while the rest are mostly intradural extramedullary tumors.¹¹ The majority of these tumors are benign, but a small percentage can present as borderline or malignant

lesions, defined as grade II or III according to the World Health Organization (WHO) classification.²²

Spinal meningiomas can be asymptomatic and diagnosed incidentally; however, they can also present with symptoms of spinal cord compression including pain and impairment in motor or sensory function.¹² Treatment strategies include observation (active surveillance),

ABBREVIATIONS EBRT = external beam radiotherapy; NCDB = National Cancer Database; SRS = stereotactic radiosurgery.

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FIG. 1. Flowchart of patient selection and treatment stratification.

excision, radiotherapy, radiosurgery, or a combination of modalities.¹⁸ Surgery continues to be the most frequently utilized treatment modality, but radiotherapy is also an option most commonly reserved for high-grade or recurrent lesions.¹⁷ Existing literature on the role of radiotherapy and radiosurgery for spinal meningioma is limited to single-institution studies, which have purported a beneficial role of radiosurgery in terms of both local control and symptom relief.²⁴ However, there remains a paucity of literature on the true rate of the use of radiotherapy for spinal meningioma and its impact on overall survival.

In light of this knowledge gap, we performed an analysis based on a national database including patients diagnosed with spinal meningioma to evaluate national utilization trends for radiotherapy and radiosurgery and investigate possible factors associated with their use. We also aimed to determine if radiotherapy alone or combined with surgery confers an overall survival benefit as compared to that obtained with surgery alone.

Methods

Data Source and Patient Cohort

The National Cancer Database (NCDB) was queried for patients in whom spinal meningioma had been diagnosed between 2004 and 2015 and who had received any type of radiation treatment. The NCDB, one of the largest cancer registries in the United States, contains almost 34 million cases from over 1500 hospitals. Data are collected

from selected health registries accredited by the American College of Surgeons' Commission on Cancer (<https://www.facs.org/quality%20programs/cancer/coc>).

We used the ICD-O-3 histological codes designating meningioma (9530–9535 and 9537–9539) and ICD-O-3 topographical codes for spinal meninges (C70.1), spinal cord (C72.0), and cauda equina (C72.1) to identify pertinent cases. The NCDB Participant User Data File consists of de-identified cases and is therefore exempt from institutional review board approval.

Outcomes of Interest

Type of treatment constituted the primary outcome of interest. Patients were classified as 1) undergoing observation only (no surgery or radiation received), 2) undergoing surgery, or 3) receiving radiation alone as the primary treatment (with no surgery at the primary site). In a separate analysis, we further stratified patients in the second category (surgery) as those who underwent surgery alone and those who received radiation in addition to surgery. Furthermore, we took into account the sequence of radiotherapy administration and performed a stratified analysis for the adjuvant mode of radiotherapy. Baseline patient characteristics, hospital characteristics, and tumor characteristics were analyzed for each group.

Covariates

The following variables were recorded: 1) patient

TABLE 1. Baseline characteristics of patients undergoing radiation treatment

Variable	Adjuvant Radiation	Radiation Only	Radiation + Surgery
No. of patients	128	131	137
Median age in yrs (range)	56 (9–86)	71 (14–90)	56 (9–88)
Female sex, no. (%)	87 (68.0)	94 (71.8)	93 (67.9)
Median FU time in mos (range)	50.5 (3.6–151.0)	48.3 (0.39–124)	52.0 (3.6–151)
Race, no. (%)			
White	103 (80.5)	112 (85.5)	109 (79.6)
African American	22 (17.2)	14 (10.6)	23 (16.8)
Other	2 (1.6)	4 (3.1)	3 (2.2)
Unknown	1 (0.8)	1 (0.8)	2 (1.5)
Charlson-Deyo Comorbidity Index, no. (%)			
0	102 (79.7)	105 (80.2)	111 (81.0)
1	14 (10.9)	21 (16.0)	14 (10.2)
2	12 (9.4)	5 (3.8)	12 (8.8)
Insurance status, no. (%)			
Not insured	2 (1.6)	3 (2.3)	2 (1.5)
Private insurance	78 (60.9)	43 (32.8)	83 (60.6)
Medicaid	13 (10.2)	4 (3.1)	13 (9.5)
Medicare	33 (25.8)	74 (56.5)	37 (27.0)
Other government	0 (0)	4 (3.1)	0 (0)
Unknown	2 (1.6)	3 (2.3)	2 (1.5)
Facility type, no. (%)			
Community Cancer Program	3 (2.3)	6 (4.6)	4 (2.9)
Comprehensive Community Cancer Program	26 (20.3)	53 (40.5)	27 (19.7)
Academic/research program	56 (43.8)	49 (37.4)	60 (43.8)
Integrated Network Cancer Program	16 (12.5)	20 (15.3)	17 (12.4)
Unknown	27 (21.1)	3 (2.3)	29 (21.2)
Tumor size in largest dimension in cm, no. (%)			
<1	3 (2.3)	12 (9.2)	3 (2.2)
1 to <2	11 (8.6)	43 (32.8)	12 (8.8)
2 to <3	21 (16.4)	25 (19.1)	23 (16.8)
3 to <4	10 (7.8)	10 (7.6)	10 (7.3)
4 to <5	11 (8.6)	3 (2.3)	11 (8.0)
5 to <6	8 (6.3)	4 (3.1)	8 (5.8)
≥6	8 (6.3)	9 (6.9)	9 (6.6)
Data missing	56 (43.8)	25 (19.1)	61 (44.5)
Tumor behavior, no. (%)			
Benign	75 (58.6)	129 (98.5)	81 (59.1)
Borderline	35 (27.3)	1 (0.8)	37 (27.0)
Malignant	18 (14.1)	1 (0.8)	19 (13.9)
Type of radiotherapy, no. (%)			
EBRT	99 (77.3)	51 (38.9)	105 (76.6)
Radiosurgery	29 (22.7)	80 (61.1)	31 (22.6)
Brachytherapy	0 (0)	0 (0)	1 (0.7)
Mean radiation dose in Gy (SD)			
EBRT	50.4 (5–540)	30 (6–100)	50.4 (2.5–540)
Radiosurgery	24 (2.1–200)	24 (8–100)	24 (10–200)

FU = follow-up.

FIG. 2. Utilization rate of radiation alone (upper) and adjuvant radiation (lower) for spinal meningioma in 2004–2015.

demographics: age (< 50, 50–69, > 69 years), sex, race, Charlson-Deyo Comorbidity Index,⁶ insurance status, and year of diagnosis; 2) type of reporting facility; 3) tumor size, grade, and behavior; and 4) treatment parameters: surgical treatment, additional radiotherapy, and type and timing of radiotherapy.

Statistical Analysis

Descriptive statistics are presented as the mean and standard deviation or the median and range for continuous variables and frequency and percentages for categorical variables.

Multivariable logistic regression analysis was performed to determine the factors associated with different treatment modalities while adjusting for age, sex, race, tumor size, and tumor behavior. We divided our analyses into three different models: model 1, fitted to predict the primary treatment modality “radiation only” versus sur-

gery or observation (dichotomous); model 2, fitted to predict the use of radiation in addition to surgery regardless of the sequence of administration (subsetting of the data set for those who underwent surgery); model 3, fitted to predict utilization of “adjuvant radiation” following surgery (subsetting of the data set for those who underwent primary surgery with no prior treatment). While performing an analysis with adjuvant radiation as the primary outcome, the extent of resection was also included as a covariate. Patients whose surgery or radiation status was classified as unknown were excluded from the analysis.

In addition, Kaplan-Meier analysis was performed to assess the impact of adjuvant radiation on survival following surgery for atypical/malignant spinal meningiomas. We also performed multivariate Cox regression to adjust for age, sex, Charlson-Deyo Comorbidity Index, tumor size, tumor behavior, and extent of resection. To avoid overfitting, we did not add more than one predictor for every 10 outcome events (deaths) in the Cox regres-

TABLE 2. Characteristics of patients receiving radiation alone

Variable	EBRT	SRS	Total	p Value
No. of patients	51	80	131	
Age in yrs				0.003
<50	3 (5.9%)	8 (10.0%)	11 (8.4%)	
>69	36 (70.6%)	32 (40.0%)	68 (51.9%)	
50–69	12 (23.5%)	40 (50.0%)	52 (39.7%)	
Sex				0.576
Male	13 (25.5%)	24 (30.0%)	37 (28.2%)	
Female	38 (74.5%)	56 (70.0%)	94 (71.8%)	
Race				0.342*
Non-Hispanic white	37 (72.5%)	67 (83.8%)	104 (79.4%)	
Hispanic	5 (9.8%)	2 (2.5%)	7 (5.3%)	
Non-Hispanic Asian/Pacific Islander	2 (3.9%)	2 (2.5%)	4 (3.1%)	
Non-Hispanic black	6 (11.8%)	8 (10.0%)	14 (10.7%)	
Other/unknown, non-Hispanic	1 (2.0%)	1 (1.2%)	2 (1.5%)	
Yr of diagnosis				0.839*
2004	3 (5.9%)	4 (5.0%)	7 (5.3%)	
2005	3 (5.9%)	5 (6.3%)	8 (6.1%)	
2006	2 (3.9%)	5 (6.3%)	7 (5.3%)	
2007	3 (5.9%)	7 (8.8%)	10 (7.6%)	
2008	7 (13.7%)	8 (10.0%)	15 (11.5%)	
2009	5 (9.8%)	11 (13.8%)	16 (12.2%)	
2010	5 (9.8%)	8 (10.0%)	13 (9.9%)	
2011	4 (7.8%)	6 (7.5%)	10 (7.6%)	
2012	6 (11.8%)	7 (8.8%)	13 (9.9%)	
2013	5 (9.8%)	7 (8.8%)	12 (9.2%)	
2014	6 (11.8%)	3 (3.8%)	9 (6.9%)	
2015	2 (3.9%)	9 (11.3%)	11 (8.4%)	
Insurance status				0.034*
Medicare	30 (58.8%)	44 (55.0%)	74 (56.5%)	
Uninsured	2 (3.9%)	1 (1.3%)	3 (2.3%)	
Private	12 (23.5%)	31 (38.8%)	43 (32.8%)	
Medicaid	4 (7.8%)	0 (0.0%)	4 (3.1%)	
Other/unknown	3 (5.9%)	4 (5.0%)	7 (5.3%)	
Tumor size†				0.976
<3 cm	29 (78.4%)	50 (62.5%)	79 (78.2%)	
>3 cm	8 (21.6%)	14 (17.5%)	22 (21.8%)	

Boldface type indicates statistical significance.

* Fisher's exact test was utilized.

† Data missing for 14 EBRT cases and 16 SRS cases.

TABLE 3. Characteristics of patients undergoing adjuvant radiotherapy

Variable	EBRT	SRS	Total	p Value
No. of patients	93	33	126	
Age in yrs				0.838
<50	36 (38.7%)	11 (33.3%)	47 (37.3%)	
>69	17 (18.3%)	6 (18.2%)	23 (18.3%)	
50–69	40 (43.0%)	16 (48.5%)	56 (44.4%)	
Sex				0.84
Male	30 (32.3%)	10 (30.3%)	40 (31.7%)	
Female	63 (67.7%)	23 (69.7%)	86 (68.3%)	
Race				0.26*
Non-Hispanic white	68 (73.1%)	19 (57.6%)	87 (69.0%)	
Hispanic	3 (3.2%)	2 (6.1%)	5 (4.0%)	
Non-Hispanic Asian/Pacific Islander	1 (1.1%)	1 (3.0%)	2 (1.6%)	
Non-Hispanic black	15 (16.1%)	6 (18.2%)	21 (16.7%)	
Other/unknown, non-Hispanic	6 (6.5%)	5 (15.2%)	11 (8.7%)	
Yr of diagnosis				0.66*
2004	4 (4.3%)	3 (9.1%)	7 (5.6%)	
2005	5 (5.4%)	1 (3.0%)	6 (4.8%)	
2006	4 (4.3%)	3 (9.1%)	7 (5.6%)	
2007	6 (6.5%)	2 (6.1%)	8 (6.3%)	
2008	7 (7.5%)	2 (6.1%)	9 (7.1%)	
2009	9 (9.7%)	1 (3.0%)	10 (7.9%)	
2010	11 (11.8%)	2 (6.1%)	13 (10.3%)	
2011	10 (10.8%)	3 (9.1%)	13 (10.3%)	
2012	4 (4.3%)	3 (9.1%)	7 (5.6%)	
2013	5 (5.4%)	5 (15.2%)	10 (7.9%)	
2014	10 (10.8%)	3 (9.1%)	13 (10.3%)	
2015	18 (19.4%)	5 (15.2%)	23 (18.3%)	
Insurance status				0.93*
Medicare	25 (26.9%)	9 (27.3%)	34 (27.0%)	
Uninsured	2 (2.2%)	0 (0.0%)	2 (1.6%)	
Private	55 (59.1%)	20 (60.6%)	75 (59.5%)	
Medicaid	10 (10.8%)	3 (9.1%)	13 (10.3%)	
Other/unknown	1 (1.1%)	1 (3.0%)	2 (1.6%)	
Tumor size†				0.12
<3 cm	29 (54.7%)	6 (33.3%)	35 (49.3%)	
>3 cm	24 (45.3%)	12 (66.7%)	36 (50.7%)	
Extent of resection‡				0.36
GTR	37 (63.8%)	11 (52.4%)	48 (60.8%)	
Biopsy/STR	21 (36.2%)	10 (47.6%)	31 (39.2%)	

GTR = gross-total resection; STR = subtotal resection.

Two cases that received proton beam radiotherapy are not included.

* Fisher's exact test for count data.

† Tumor size was missing in 40 EBRT cases and 15 SRS cases.

‡ Extent of resection was missing in 35 EBRT cases and 12 SRS cases.

sion model. Patients diagnosed in the year 2015 were excluded from survival analysis given the lack of follow-up regarding vital status. For all analyses, the level of statistical significance was established at $p < 0.05$. All statistical analyses were performed using R statistical software version 3.4.1 (R Foundation for Statistical Computing; <https://www.R-project.org/>).

TABLE 4. Multivariable analysis for factors associated with increased utilization of each treatment modality

Variable	Radiation Only (n = 131)		Any Radiation + Surgery (n = 137)		Adjuvant Radiation (n = 128)	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Tumor size in cm						
1 to <2	Reference		Reference		Reference	
<1	1.29 (0.66–2.53)	0.46	2.44 (0.66–8.98)	0.18	2.67 (0.72–9.85)	0.14
2 to <3	0.93 (0.56–1.53)	0.77	2.51 (1.23–5.15)	0.01	2.28 (1.10–4.74)	0.03
3 to <4	1.83 (0.91–3.70)	0.09	4.32 (1.78–10.5)	0.00	4.40 (1.81–10.7)	0.001
4 to <5	1.76 (0.53–5.83)	0.35	19.2 (7.65–48.4)	<0.001	17.4 (6.73–44.7)	<0.001
5 to <6	4.87 (1.63–14.5)	<0.001	23.0 (7.66–69.2)	<0.001	23.5 (7.76–71.1)	<0.001
≥6	2.33 (0.9–6.1)	0.08	8.17 (2.95–22.63)	<0.001	7.36 (2.51–21.5)	<0.001
Missing data	0.52 (0.32–0.83)	0.01	3.45 (1.82–6.55)	<0.001	3.24 (1.70–6.18)	<0.001
Age						
<50	Reference		Reference		Reference	
50–69	2.36 (1.21–4.61)	0.01	0.89 (0.58–1.37)	0.61	0.96 (0.62–1.50)	0.87
>69	3.51 (1.67–7.39)	<0.001	0.70 (0.36–1.37)	0.30	0.74 (0.37–1.48)	0.39
Sex						
Male	Reference		Reference		Reference	
Female	0.64 (0.43–0.95)	0.03	0.76 (0.51–1.14)	0.18	0.80 (0.52–1.21)	0.29
Race						
White	Reference		Reference		Reference	
Hispanic	1.26 (0.57–2.76)	0.57	0.85 (0.35–2.06)	0.71	0.74 (0.28–1.95)	0.55
African American	1.57 (0.88–2.80)	0.12	2.19 (1.29–3.73)	0.004	2.05 (1.18–3.54)	0.01
Asian/Pacific Islander	0.95 (0.35–2.62)	0.93	0.64 (0.19–2.13)	0.47	0.45 (0.10–1.90)	0.27
Other/unknown	0.22 (0.05–0.89)	0.03	1.41 (0.75–2.66)	0.29	1.24 (0.63–2.45)	0.53
Charlson-Deyo Comorbidity Index						
0	Reference		Reference		Reference	
1	0.71 (0.44–1.14)	0.16	0.53 (0.29–0.97)	0.04	0.57 (0.31–1.03)	0.06
≥2	0.30 (0.12–0.75)	0.01	0.80 (0.42–1.52)	0.49	0.84 (0.44–1.63)	0.62
Insurance status						
Medicare	Reference		Reference		Reference	
Uninsured	0.95 (0.35–2.62)	0.93	0.43 (0.09–2.01)	0.28	0.49 (0.10–2.32)	0.37
Private	0.98 (0.61–1.58)	0.94	1.60 (0.95–2.71)	0.08	1.69 (0.97–2.92)	0.06
Medicaid	0.77 (0.26–2.22)	0.63	2.00 (0.92–4.37)	0.08	2.35 (1.06–5.19)	0.03
Other/unknown	2.44 (1.08–5.54)	0.03	0.80 (0.18–3.50)	0.77	0.89 (0.20–3.94)	0.88
Yr of diagnosis						
2004	Reference		Reference		Reference	
2005	0.99 (0.36–2.77)	0.99	0.99 (0.35–2.84)	0.99	1.36 (0.45–4.16)	0.59
2006	0.90 (0.31–2.60)	0.85	0.98 (0.36–2.68)	0.97	1.02 (0.33–3.17)	0.97
2007	1.27 (0.48–3.37)	0.63	1.16 (0.42–3.21)	0.78	1.57 (0.53–4.68)	0.42
2008	1.59 (0.64–3.96)	0.32	1.25 (0.48–3.27)	0.64	1.37 (0.47–4.00)	0.56
2009	1.72 (0.70–4.25)	0.24	1.43 (0.54–3.78)	0.47	1.96 (0.69–5.57)	0.20
2010	1.35 (0.53–3.44)	0.53	1.96 (0.78–4.93)	0.15	1.58 (0.13–19.9)	0.72
2011	0.99 (0.37–2.62)	0.98	1.50 (0.59–3.79)	0.39	1.35 (0.11–17.3)	0.82
2012	1.17 (0.46–2.97)	0.74	1.00 (0.34–2.94)	0.99	0.9 (0.07–12.0)	0.94
2013	1.09 (0.42–2.81)	0.86	1.36 (0.52–3.57)	0.54	1.33 (0.10–17.2)	0.83
2014	0.72 (0.26–1.95)	0.52	1.76 (0.71–4.37)	0.22	1.63 (0.13–20.4)	0.71
2015	0.92 (0.35–2.42)	0.87	3.26 (1.14–7.56)	0.01	3.26 (0.27–39.3)	0.35
Behavior						
Benign	Reference		Reference		Reference	
Borderline	0.28 (0.04–2.09)	0.22	12.4 (7.89–19.5)	<0.001	13.4 (8.35–21.4)	<0.001

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TABLE 4. Multivariable analysis for factors associated with increased utilization of each treatment modality

Variable	Radiation Only (n = 131)		Any Radiation + Surgery (n = 137)		Adjuvant Radiation (n = 128)	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Behavior (<i>continued</i>)						
Malignant	0.77 (0.10–5.70)	0.80	21.3 (11.6–39.2)	<0.001	24.0 (12.8–45.1)	<0.001
Extent of resection						
GTR	Reference		Reference		Reference	
No GTR	NA	NA	NA	NA	2.77 (1.66–4.62)	<0.001
Unknown	NA	NA	NA	NA	0.92 (0.09–9.94)	0.94

NA = not applicable.

Boldface type indicates statistical significance.

Results

Demographic and Treatment Characteristics

Among all patients who had received radiation, 131 (48.9%) had radiation alone and 137 (51.1%) had radiation in addition to surgery (Fig. 1). Patients who had radiation alone had a median age of 71 years (range 14–90 years) and those who received radiation in addition to surgery had a median age of 56 years (range 9–88 years). Median follow-up times for radiation alone and surgery plus radiation were 48.3 months (range 0.39–124 months) and 52.0 months (range 3.6–151 months), respectively. Patients who received adjuvant radiation had a median age of 56 years (range 9–86 years) and a median follow-up of 50.5 months (range 3.6–151.0 months). Baseline characteristics of the patients are presented in Table 1.

Tumor and Treatment Characteristics

For patients who received radiation alone, the majority of tumors (43 [32.8%]) had diameters from 1 to < 2 cm, followed by tumors with diameters from 2 to < 3 cm (25 [19.1%]). Among patients who received radiation plus surgery and patients undergoing adjuvant radiation, the majority of tumors had diameters from 2 to < 3 cm (23 [16.8%] and 21 [16.4%], respectively). Radiosurgery was the most common radiation treatment in the patients receiving radiation alone (80 [61.1%]), whereas external beam radiotherapy (EBRT) was the preferred method for patients undergoing radiation therapy plus surgery (105 [76.6%]). Tumor and treatment characteristics can be found in more detail in Table 1.

Yearly Utilization of Radiation

The utilization rates for radiation only and adjuvant radiation were calculated for each year, starting from 2004 until 2015. The rate was calculated as the number of cases receiving adjuvant radiation or radiation alone divided by all cases of spinal meningioma in a given year. The utilization rate for radiation alone was 1.02% in 2004 and 1.12% in 2015 with small fluctuations in between. In contrast, adjuvant radiation had a utilization rate of 1.02% in 2004 and 2.54% in 2015, mostly showing a trend toward an increase in utilization. Separate assessment for the utilization of EBRT and stereotactic radiosurgery (SRS) showed an increasing trend for SRS in the patients receiving radia-

tion alone, whereas EBRT was the method of choice for patients undergoing adjuvant radiation therapy. A graphic view of utilization rates is presented in Fig. 2.

Multivariable Analysis for Factors Predicting the Use of Radiotherapy

Tables 2 and 3 summarize the characteristics of patients receiving radiation alone versus adjuvant radiation. On multivariable analysis, we found age > 69 years ($p < 0.001$), male sex ($p = 0.03$), and tumor size from 5 to < 6 cm ($p < 0.001$) to be associated with significantly higher odds of receiving radiation only and a Charlson-Deyo Comorbidity Index ≥ 2 ($p = 0.01$) to be associated with significantly lower odds of receiving radiation alone. In addition, a larger lesion size (2 to < 3 cm, $p = 0.01$; 3 to < 4 cm, $p < 0.001$, 4 to < 5 cm, $p < 0.001$, 5 to < 6 cm, $p < 0.001$ and ≥ 6 cm, $p < 0.001$; reference = 1 to < 2 cm) and borderline ($p < 0.001$) and malignant tumors ($p < 0.001$) were associated with increased odds of receiving radiation in addition to surgery. In a stratified analysis restricted to patients undergoing primary surgery with no prior treatment, larger tumor size and borderline or malignant tumor behavior were associated with increased odds of adjuvant radiation. In addition, patients undergoing subtotal resection were also more likely to receive adjuvant radiation ($p < 0.001$). In all models, we did not encounter an increase in the use of radiotherapy during successive years (as compared to 2004). Table 4 summarizes the results of all multivariable analyses predicting the use of radiotherapy.

Impact of Adjuvant Radiation on Overall Survival for Atypical Tumors

Among the patients with borderline or malignant tumors, univariate log-rank statistics demonstrated lower survival in those receiving adjuvant radiotherapy compared to those undergoing surgery alone (5-year survival: 66% vs 86%, $p < 0.001$, log-rank; Fig. 3A). These findings were confirmed on a multivariable Cox proportional hazards analysis adjusting for age, sex, tumor size and behavior, and extent of resection, showing a higher risk of mortality with radiation (HR 2.12, 95% CI 1.02–4.1, $p = 0.02$, reference = no radiation). In an analysis further stratifying tumors with malignant behavior only, although a worse 5-year survival rate was noted with adjuvant radiotherapy

FIG. 3. Kaplan-Meier survival curves depicting overall survival in patients with borderline or malignant spinal meningiomas (A) and in patients with malignant meningiomas (B) who did or did not receive adjuvant radiation following surgery.

TABLE 5. Cox proportional hazards analysis for the impact of adjuvant radiation on mortality in patients with borderline or malignant tumors

Variable	Borderline or Malignant (n = 308)		Malignant Only (n = 88)	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age	1.03 (1.01–1.10)		0.98 (0.96–1.01)	0.34
Sex			—	—
Female	Reference			
Male	1.86 (1.02–3.1)	0.04	1.96 (0.7–5.8)	0.22
Extent of resection			—	—
GTR	Reference			
No GTR	0.23 (0.03–1.7)	0.15		
Unknown	0.74 (0.38–1.4)	0.37		
Tumor size			—	—
<3 cm	Reference			
>3 cm	1.11 (0.51–2.5)	0.79		
Missing data	1.14 (0.60–2.2)	0.69		
Radiation			—	—
No	Reference		Reference	
Yes	2.12 (1.02–4.1)	0.02	1.18 (0.39–3.7)	0.77
Behavior				
Borderline	Reference		—	—
Malignant	1.77 (1.01–4.1)	0.04		

n = number of patients.

Boldface type indicates statistical significance. No more than one predictor was added for every 10 outcome events. Data on tumor size and extent of resection were missing in 42 and 54 cases, respectively, precluding inclusion in the model.

(62% vs 79%), log-rank comparison did not show a statistically significant difference in survival ($p = 0.13$; Fig. 3B). Cox proportional hazards analysis (adjusted for age and extent of resection) also did not demonstrate a significant difference in mortality (HR 1.18, 95% CI 0.39–3.7, $p = 0.77$, reference = no radiation). Table 5 summarizes the results of the adjusted Cox analysis.

Discussion

The current analyses of 268 patients with spinal meningiomas from a national cancer database revealed no significant changes in the trends of radiation use over the last decade. Moreover, tumor size and behavior (benign, borderline, or malignant) were found to be the most prominent factors associated with the involvement of radiation in overall management. We also found that patients who received radiation as an adjunct to surgery were more likely to receive EBRT, whereas those receiving radiation as the only treatment were more likely to undergo SRS.

Agarwal et al. reported on an analysis of the Surveillance, Epidemiology, and End Results (SEER) Program, in which they evaluated trends in the management of cranial meningioma.¹ In contrast to our findings, an increasing inclination toward radiotherapy was seen as the years progressed.¹ Moreover, Agarwal and colleagues noted a

higher utilization of surgery for larger tumors. We noted a similar trend for the use of both surgery and radiation for larger tumor sizes in spinal meningiomas.

Although the literature on spinal meningiomas is not as extensive as that on cranial meningiomas, it is generally accepted that resection is the main modality for first-line management.⁵ In contrast, the use of radiation in addition to surgery in the management of meningiomas is reported as the treatment of choice for recurrent tumors.^{14,21,23} Moreover, radiotherapy/radiosurgery after resection has been reported for large or atypical/anaplastic tumors.^{13,16,26} Adjuvant radiotherapy has also been used among patients with spinal meningioma who had a concurrent or previous cranial meningioma.¹⁹ Results from the present study are consistent with the previous literature, showing increased odds of radiation use with tumors that are larger and with borderline or malignant behavior.¹⁹

Radiation as a sole treatment for meningiomas has also been reported and is hypothesized to provide outcomes comparable to those obtained with surgery.⁷ Radiation can prove to be a feasible treatment option, especially in cases in which complete resection is not possible because of anatomical difficulty in surgical access. Kufeld et al. reported on a series of 11 patients with WHO grade I spinal meningioma who were treated with radiotherapy only.¹⁵ After a follow-up period of 18 months, no progression was detected and there were no myelopathic signs. Similarly, Pandit et al. described an analysis of 16 patients with optic nerve sheath meningioma, revealing significant improvement in patients' visual function and suggesting radiotherapy as an alternative to surgery.²⁰ Overall, among the available techniques, radiosurgery is reported in the literature more frequently than EBRT, which is consistent with the current analysis.^{3,4}

Finally, we found insufficient evidence to conclude that the addition of adjuvant radiation to overall management confers a survival benefit for patients with borderline or malignant tumors. However, significant improvements in progression-free survival have been noted with the use of radiation in previous studies.¹⁹ Since the NCDB does not capture recurrence, progression-free survival could not be assessed in our study.

Study Limitations

There are limitations to the present study. First, among the 10,458 patients with spinal meningioma in the database, we found only 268 patients who had received radiotherapy or undergone radiosurgery. Tumor size and extent of resection were also missing for a significant number of cases. Therefore, our findings could be limited by a type I error. Second, the NCDB does not record recurrence, toxicity, and other patient-reported outcomes, which are pertinent factors in deciding on management. It is well reported in the literature that radiation is frequently utilized in the management of recurrent meningiomas.²⁵ However, given a lack of information, we could not determine the impact of radiation on progression-free survival. Radiation toxicity and related patient-reported outcomes are important measures to assess the feasibility of radiation use in any oncological condition.^{9,10} Radiation-induced myelopathy is an important complication that warrants further

investigation.⁸ Third, we could not study cause-specific mortality, as that is not available in the NCDB. Although meningioma is not associated with high rates of mortality, disease-specific mortality is an important outcome to assess, and the lack of this variable limits our ability to make conclusive recommendations.

Conclusions

A study of patients with spinal meningiomas from a national cancer database revealed a small increase in the utilization of radiation for the management of spinal meningioma without a significant increase in overall survival. Larger tumor size and borderline or malignant behavior were found to be associated with increased radiation use. Further studies assessing the efficiency of radiation in the management of atypical or anaplastic meningiomas should be performed to better understand the role of radiation in the management of spinal meningiomas.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Yolcu, Goyal. Acquisition of data: Yolcu, Goyal. Analysis and interpretation of data: Yolcu, Goyal, Alvi. Drafting the article: Yolcu, Goyal, Alvi, Moinuddin. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Bydon. Statistical analysis: Yolcu, Goyal, Alvi. Administrative/technical/material support: Bydon. Study supervision: Bydon.

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