Morbidity and Mortality Associated With Meningioma After Cranial Radiotherapy: A Report From the Childhood Cancer Survivor Study

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Journal Title: Journal of Clinical Oncology
Volume: Volume 35, Number 14
Publisher: American Society of Clinical Oncology | 2017-05-10, Pages 1570-1576
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1200/JCO.2016.70.1896
Permanent URL: https://pid.emory.edu/ark:/25593/s9pzb

Final published version: http://dx.doi.org/10.1200/JCO.2016.70.1896

VOLUME 35 · NUMBER 14 · MAY 10, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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Published at jco.org on March 24, 2017.

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0732-183X/17/3514w-1570w/$20.00

A B S T R A C T

Purpose

Little is known about neurologic morbidity attributable to cranial radiotherapy (CRT) –associated meningiomas.

Materials and Methods

From 4,221 survivors exposed to CRT in the Childhood Cancer Survivor Study, a diagnosis of meningioma and onset of neurologic sequelae were ascertained. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% CIs to evaluate the factors associated with neurologic sequelae after subsequent meningioma.

Results

One hundred ninety-nine meningiomas were identified among 169 participants. The median interval from primary cancer to meningioma diagnosis was 22 years (5 to 37 years). The cumulative incidence of a subsequent meningioma by age 40 years was 5.6% (95% CI, 4.7% to 6.7%). CRT doses of 20 to 29.9 Gy (HR, 1.6; 95% CI,1.0 to 2.6) and doses ≥ 30 Gy (HR, 2.6; 95% CI, 1.6 to 4.2) were associated with an increased risk of meningioma compared with CRT doses of 1.5 to 19.9 Gy ($P < .001$). Within 6 months before or subsequent to a meningioma diagnosis, 20% (30 of 149) reported at least one new neurologic sequela, including seizures (8.3%), auditory-vestibular-visual deficits (6%), focal neurologic dysfunction (7.1%), and severe headaches (5.3%). Survivors reporting a meningioma had increased risks of neurologic sequelae > 5 years after primary cancer diagnosis, including seizures (HR, 10.0; 95% CI, 7.0 to 15.3); auditory-vestibular-visual sensory deficits (HR, 2.3; 95% CI, 1.3 to 4.0); focal neurologic dysfunction (HR, 4.9; 95% CI, 3.2 to 7.5); and severe headaches (HR, 3.2; 95% CI, 1.9 to 5.4). With a median follow-up of 72 months after meningioma diagnosis (range, 3.8 to 395 months), 22 participants (13%) were deceased, including six deaths attributed to a meningioma.

Conclusion

Childhood cancer survivors exposed to CRT and subsequently diagnosed with a meningioma experience significant neurologic morbidity.

J Clin Oncol 35:1570-1576. © 2017 by American Society of Clinical Oncology

INTRODUCTION

Meningiomas and high-grade gliomas are the most common subsequent neoplasms that occur in the CNS among childhood cancer survivors exposed to cranial radiotherapy (CRT).[1-7] Notably, unlike the incidence of high-grade glioma, the cumulative incidence of subsequent meningiomas after CRT does not seem to reach a plateau over time.[1,5,8-11] Thus, meningiomas are the most common subsequent CNS tumors among aging adult survivors of childhood cancer.[1,5,7,10] Fortunately, given the benign nature of most meningiomas, cancer survivors with subsequent meningiomas have higher survival rates than do those with subsequent high-grade gliomas.[7,9,12,13]

Periodic screening of childhood cancer survivors treated with CRT has been proposed to facilitate earlier diagnosis of subsequent meningiomas with a goal of potentially reducing presurgical and surgery-related morbidity and premature deaths. However, meningioma-related morbidity and mortality have not been well characterized, and therefore, the potential benefit of screening is not known.[14-16] A better

DOI: 10.1200/JCO.2016.70.1896

understanding of meningioma-related morbidity and mortality is essential to develop informed screening recommendations. The primary aims of this study were to characterize the neurologic sequelae associated with subsequent meningiomas and to examine all-cause mortality among childhood cancer survivors who develop subsequent to these meningiomas.

MATERIALS AND METHODS

Study Population

The Childhood Cancer Survivor Study (CCSS) is a retrospective cohort study with longitudinal follow-up of survivors of childhood cancer treated at 26 institutions in the United States and Canada. Eligibility for participation in the CCSS included diagnosis of cancer before age 21 years, initial treatment between 1970 and 1986, and being alive 5 years after diagnosis of leukemia, CNS tumor, Hodgkin or non-Hodgkin lymphoma, Wilms tumor, neuroblastoma, soft tissue sarcoma, or bone tumor. The cohort methodology and study design have been described previously.[17,18] The CCSS was approved by institutional review boards at the participating centers. Participants provided informed consent. Analysis for this study was restricted to participants who were treated with CRT within 5 years of their primary cancer diagnosis. Of the CCSS participants, 4,221 met these criteria.

Ascertainment of Treatment Information

The primary childhood cancer diagnosis and therapeutic exposures were abstracted from medical records obtained from treating institutions. Radiation therapy records, including calculated body region dosimetry of maximum CRT dose as both initial therapy and for recurrent disease within 5 years of the primary cancer diagnosis, were examined.

Identification and Confirmation of Meningiomas

Meningiomas were identified initially through self- or proxy report. They were confirmed by pathology reports if available or alternatively, by other medical records. Subjects with multiple meningiomas were included in the analysis.

Identification of Neurologic Outcomes

All participants completed a baseline survey (administered between 1994 and 1999) that included demographics, personal and family medical history, and an assessment of chronic health conditions. A proxy (parent, spouse, or next of kin) completed the baseline survey for survivors who died $>$ 5 years after diagnosis, who were under age 18 years, or who were unable to complete the survey. Subsequently, there have been periodic follow-up surveys. Study surveys can be viewed at http://ccss.stjude.org. Survey questions regarding neurologic conditions examined auditory-vestibular-visual sensory deficits, focal neurologic dysfunction, pain, and seizures. Questions began with the phrase, "Have you ever been told by a doctor or other health care professional that you have or have had [specific condition]?" If participants gave a yes response, they were then asked their age at first diagnosis.

Statistical Analysis

Survivors of childhood cancer were considered at risk of meningiomas beginning at entry into the CCSS cohort, 5 years after their childhood cancer diagnosis, until a confirmed diagnosis of meningioma, death, or date of most recent contact. Cumulative incidence of meningioma overall, by sex, by treatment exposure, and by age at diagnosis were calculated with a nonparametric estimate using age as the time scale and treating death as a competing risk.[19,20] Overall survival (OS) from diagnosis of meningioma was estimated using Kaplan-Meier methods.

Cox regression estimated the hazards of a first meningioma diagnosis, using year since CCSS study entry as the time scale, to assess variables that modify the risk of a first meningioma diagnosis. A multivariable model was constructed, starting with a full model including age at primary diagnosis, sex, ethnicity, and cranial radiation dose, and using backward elimination, retaining factors associated with the risk of a first meningioma at the $P < .20$ level.

Four types of neurologic sequelae were considered: seizure disorder, auditory-vestibular-visual sensory deficits, focal neurologic dysfunction, and headaches. A seizure disorder was defined by a report of epilepsy, repeated seizures, convulsions, or blackouts. Auditory-vestibular-visual sensory deficits included any hearing loss (defined as hearing loss requiring a hearing aid, deafness in one or both ears not corrected by a hearing aid, or complete deafness in either ear), tinnitus, persistent dizziness, legal blindness in one or both eyes, or double vision. Focal neurologic dysfunction included deficits related to balance, tremors or movement, weakness, or inability to move arm(s) or leg(s). The frequency of each neurologic sequela was summarized among patients who developed a meningioma and was depicted using histogram plots. Because CCSS surveys only captured age at first onset and not the date, each neurologic sequela was assumed to have occurred at the midpoint (ie, July 1) of the year corresponding to the reported age.

To compare the hazard of each neurologic sequela between patients who subsequently developed meningioma and those patients who did not, Cox regression was used, treating meningioma diagnosis as a time-dependent covariate. Survivors were considered to be at risk of each neurologic sequela at entry into the CCSS cohort (ie, 5 years after cancer diagnosis). Survivors who reported the onset of a neurologic sequela before this 5-year time period were excluded from the multivariate analysis of that particular sequela category. That is, only the first neurologic sequela event was recorded, and if that event occurred within 5 years of primary cancer diagnosis, no future events would have been captured. Multivariable models adjusting for known sex and cranial radiation dose are presented.

Two-sided P values $< .05$ were considered statistically significant.

RESULTS

Among the 4,221 survivors exposed to CRT in the CCSS cohort, the median age at the time of analysis was 32 years (range, 8 to 55 years). One hundred sixty-nine childhood cancer survivors were identified as having 199 subsequent meningiomas (Table 1). Survivors with subsequent meningiomas were a median age of 35 years (range, 15 to 56 years) at last follow-up. Of the 169 subjects with subsequent meningiomas, their median age at primary cancer diagnosis was 4.0 years (range, 0 to 18 years); 100 (59.2%) were female. The primary cancer diagnoses of survivors with subsequent meningiomas included leukemia (58.0%), CNS tumor (36.1%), and other cancers (5.9%). Among the 169 survivors who reported a meningioma, 85.2% reported a single meningioma and 14.8% reported two or more meningiomas (Table 1). The median age at diagnosis of the first meningioma was 28 years (range, 7 to 50 years), and the median interval from primary cancer diagnosis to first meningioma diagnosis was 22 years (range, 5 to 37 years). One hundred sixty-four subjects (97%) were diagnosed with benign meningiomas, and five subjects (3%) were diagnosed with malignant meningiomas. Among those with a subsequent meningioma, CRT doses were 1.5 to 19 Gy in 13.6%; 20 to 29.9 Gy in 42.0%; and $\geq$ 30 Gy in 44.3%.

The cumulative incidence of a subsequent meningioma was 5.6% (95% CI, 4.7% to 6.7%) by age 40 years (Fig 1A) and 5.8% (95% CI, 4.8% to 6.8%) at 30 years after primary cancer diagnosis (Data Supplement). The incidence was 7.0% (95% CI, 5.3% to

Table 1. Clinical Characteristics of Childhood Cancer Survivors Exposed to Cranial Radiotherapy Who Did and Did Not Develop Meningiomas

Characteristic	Meningioma (n = 169)	No Meningioma (n = 4052)
Median age at diagnosis of primary cancer, years	4.0 (0-18)	5.0 (0-20)
Age at original diagnosis, years		
< 5	87 (4.6)	1,800 (95.4)
5-10	53 (3.9)	1,313 (96.1)
11-14	19 (3.1)	598 (96.9)
15-20	10 (2.8)	341 (97.2)
Median age at last follow-up, years	35 (15-56)	32 (9-55)
Age at last follow-up, years		
20-29	3 (7.7)	36 (92.3)
30-39	49 (2.9)	1,667 (97.1)
≥ 40	117 (4.7)	2,349 (95.3)
Median duration of follow-up, years	22.8 (5.5-38)	25.7 (8.4-39)
Male sex	69 (3.0)	2,245 (97.0)
Ethnicity		
White, non-Hispanic	151 (4.1)	3,539 (95.9)
Black, non-Hispanic	3 (2.0)	146 (98.0)
Hispanic	7 (3.2)	209 (96.8)
Other	6 (4.0)	144 (96.0)
Missing	2 (14.3)	12 (85.7)
Primary cancer diagnosis		
Leukemia	98 (3.7)	2,536 (96.3)
CNS tumor	61 (5.7)	1,017 (94.3)
Others	10 (2.0)	499 (98.0)
Exposure to cranial radiotherapy, Gy		
1.5-19.9	23 (1.9)	1,214 (98.1)
20-29.9	71 (4.8)	1,409 (95.2)
≥ 30	75 (5.0)	1,416 (95.0)
Missing	0 (0)	13 (100)
Total No. of meningiomas/subject		
1	144 (85.2)	
2	20 (11.8)	
3	5 (3.0)	
Median age at diagnosis of meningioma, years	28 (7-50)	
Age at meningioma diagnosis, years		
< 15	4 (2.4)	
15-19	15 (8.8)	
20-24	30 (17.7)	
25-29	55 (32.3)	
30-34	32 (18.9)	
≥ 35	33 (19.5)	
Median interval from original cancer diagnosis to meningioma diagnosis, years	22 (5-37)	
Interval between primary cancer and meningioma diagnosis, years		
5-9	5 (3.0)	
10-14	15 (8.8)	
15-19	40 (23.6)	
20-24	47 (27.8)	
≥ 25	62 (36.6)	
Pathology		
Benign meningioma	164 (97.1)	
Malignant meningioma	5 (2.9)	
Cause of death among participants exposed to radiotherapy and who developed meningiomas (n = 22)		
Meningioma	6 (27.3)	
Original cancer	4 (18.2)	
Accident, homicide, or suicide	4 (18.2)	
Unknown or other	4 (18.2)	
Secondary anaplastic astrocytoma	2 (9.1)	
Cerebrovascular disease	2 (9.1)	

NOTE. Data are presented as No. (%) or No. (range).

9.0%) among women and 4.4% (95% CI, 3.3% to 5.6%) among men (Fig 1B). The cumulative incidence of meningiomas by age 40 years by CRT dose was 3.0% (95% CI, 1.9% to 4.5%), 6.3% (95% CI, 4.8% to 8.0%], and 6.2% (95% CI, 4.6% to 8.1%) for those treated with 1.5 to 19 Gy, 20 to 29.9 Gy, and ≥ 30 Gy, respectively (Fig 1C). The cumulative incidence of meningiomas by age 40 years by age at initial cancer diagnosis was 10.4% (95% CI, 7.2% to14.1%), 6.2% (95% CI, 4.5% to 8.2%), 2.7% (95% CI, 1.5% to 4.4%), and 1.5% (95% CI, 0.6% to 3.4%) for subjects' whose age at diagnosis was < 5 years, 5 to 10 years, 11 to 15 years, and > 15 years, respectively (Fig 1D).

Risk Factor Analysis for Subsequent Meningioma

Multivariable analysis identified female sex to be associated with an increased risk of meningioma (hazard ratio [HR], 1.7; 95% CI, 1.2 to 2.3; $P = .001$) (Table 2). Furthermore, CRT doses of 20 to 29.9 Gy (HR, 1.6; 95% CI, 1.0 to 2.6) and doses ≥ 30 Gy (HR, 2.6; 95% CI, 1.6 to 4.2) were associated with a higher risk of meningioma when compared with CRT doses of 1.5 to 19.9 Gy ($P < .001$). The adjusted increased risk of a meningioma for every 5 Gy in CRT dose was HR, 1.12 (95% CI, 1.06 to 1.18; $P < .001$).

Neurologic Outcomes

Of the 169 survivors diagnosed with a subsequent meningioma, 149 (88.2%) reported at least one neurologic sequela at some time point beyond 5 years from the diagnosis of the primary cancer. Among these 169 survivors, 66 (39%), 91 (53.8%), 96 (56.8%), and 91 (53.8%) reported seizures, auditory-vestibular-visual deficits, focal neurologic dysfunction, and severe headaches, respectively, after the diagnosis of meningioma. Within 6 months before or subsequent to a meningioma diagnosis, 20% (30 of 149) reported at least one new neurologic sequelae: 8.3% reported first-onset seizures; 6%, auditory-vestibular-visual deficits; 7.1%, focal neurologic dysfunction; and 5.3%, severe headaches (Fig 2). Adjusting for sex and CRT dose, survivors had an increased risk of neurologic sequelae within ± 6 months of meningioma diagnosis, including seizures (HR, 10.0; 95% CI, 7.0 to 15.3; $P < .001$), auditory-vestibular-visual sensory deficits (HR, 2.3; 95% CI, 1.3 to 4.0; $P < .01$), focal neurologic dysfunction (HR, 4.9; 95% CI, 3.2 to 7.5; $P = < .001$), and severe headaches (HR, 3.2; 95% CI, 1.9 to 5.4; $P < .001$; Table 3).

Mortality

Among patients diagnosed with a subsequent meningioma after childhood cancer, the median follow-up among survivors was 72 months (range, 3.8 to 395 months) and 22 (13%) had died (Table 1). The 3- and 5-year OS after diagnosis of a subsequent meningioma was 95% (95% CI, 90% to 97%) and 91% (95% CI, 85% to 95%), respectively (Fig 3). Six of these deaths were attributed to a meningioma.

DISCUSSION

This large cohort study demonstrates that nearly 6% of childhood cancer survivors exposed to CRT will be diagnosed subsequently

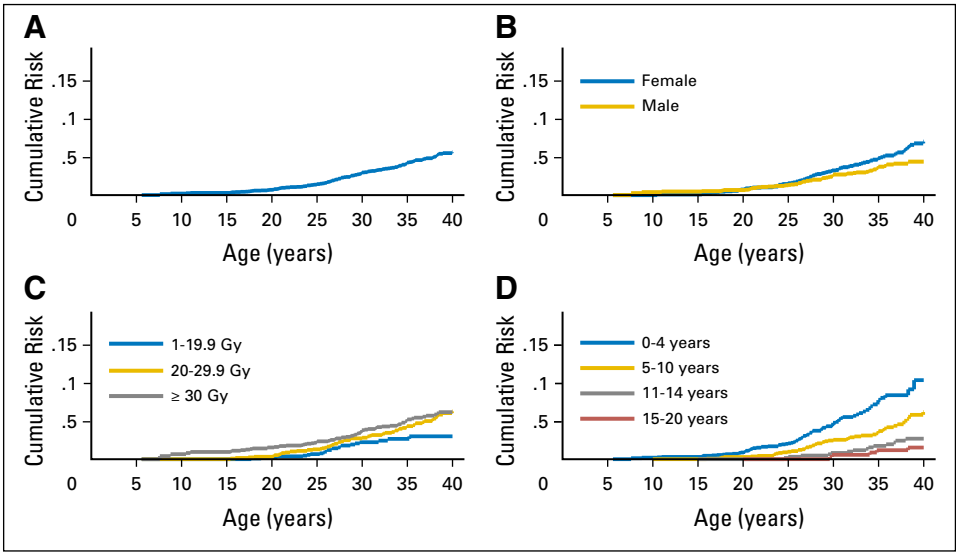

Fig 1. Cumulative incidence of subsequent meningiomas by attained age for (A) all subjects exposed to cranial radiation, (B) women versus men, (C) dose of cranial radiation, and (D) age at primary cancer diagnosis.

with a meningioma by age 40 years, with no plateau in incidence, and that diagnosis of a meningioma is associated with considerable neurologic sequelae. To our knowledge, this is the largest study of cancer survivors with subsequent meningiomas and the first study to characterize the neurologic morbidity, including first-onset seizures, auditory-vestibular-visual sensory deficits, focal neurologic dysfunction, and severe headaches, in this population. Furthermore, this study demonstrates that the onset of neurologic morbidity seems to be associated temporally with the diagnosis of a subsequent meningioma. Finally, this study demonstrates that childhood cancer survivors diagnosed with subsequent meningiomas have considerable mortality, suggesting that a diagnosis of subsequent meningiomas may be a harbinger of future problems.

Previous reports from the CCSS have observed increased rates of seizures, late-onset auditory-vestibular-visual sensory deficits, focal neurologic dysfunction, and headaches among survivors of childhood CNS tumors and leukemia.[21,22] Among CNS tumor survivors, Packer et al[21] reported that CRT was associated with increased rates of seizures, hearing impairment, and motor deficits. Similarly, Goldsby et al[22] reported increased rates of seizures, auditory-vestibular-visual deficits, focal neurologic deficits, and headaches among leukemia survivors. However, in that study of leukemia survivors, CRT dose was not associated with neurologic sequelae. In this study, in addition to being associated with higher CRT doses, the onset of neurologic sequelae was often noted to occur within 6 months before or subsequent to the diagnosis of meningioma. Given the high rate of morbidity at the time of diagnosis of a meningioma, these results warrant further evaluation of the potential risks and benefits of surveillance for meningiomas in childhood cancer survivors treated with CRT.

Table 2. Risk Factors for Subsequent Meningiomas Among Childhood Cancer Survivors Exposed to Cranial Radiation

	Univariable			Multivariable		
Characteristic	HR	95% CI	*P*	HR	95% CI	*P*
Age at primary cancer, years			.198			.076
< 5	1.5	0.8 to 3.0		1.6	0.8 to 3.2	
5-10	1.2	0.6 to 2.4		1.2	0.6 to 2.4	
11-15	0.9	0.5 to 2.1		0.9	0.4 to 2.0	
16-20	1.0	—		1.0	—	
Sex			.001			.001
Male	1.0	—		1.0	—	
Female	1.6	1.2 to 2.2		1.7	1.2 to 2.3	
Ethnicity			.776			
White, non-Hispanic	1.0	—				
Other	1.1	0.7 to 1.8				
CRT exposure, Gy			< .001			< .001
1.5-19.9	1.0	—		1.0	—	
20-29.9	1.6	1.0 to 2.6		1.6	01.0 to 2.6	
≥ 30	2.4	1.5 to 3.9		2.6	1.6 to 4.2	

NOTE. Adjusted risk of meningiomas for every incremental increase of 5 Gy was HR, 1.12 (95% CI, 1.06 to 1.18); $P < .001$.
Abbreviation: CRT, cranial radiotherapy.

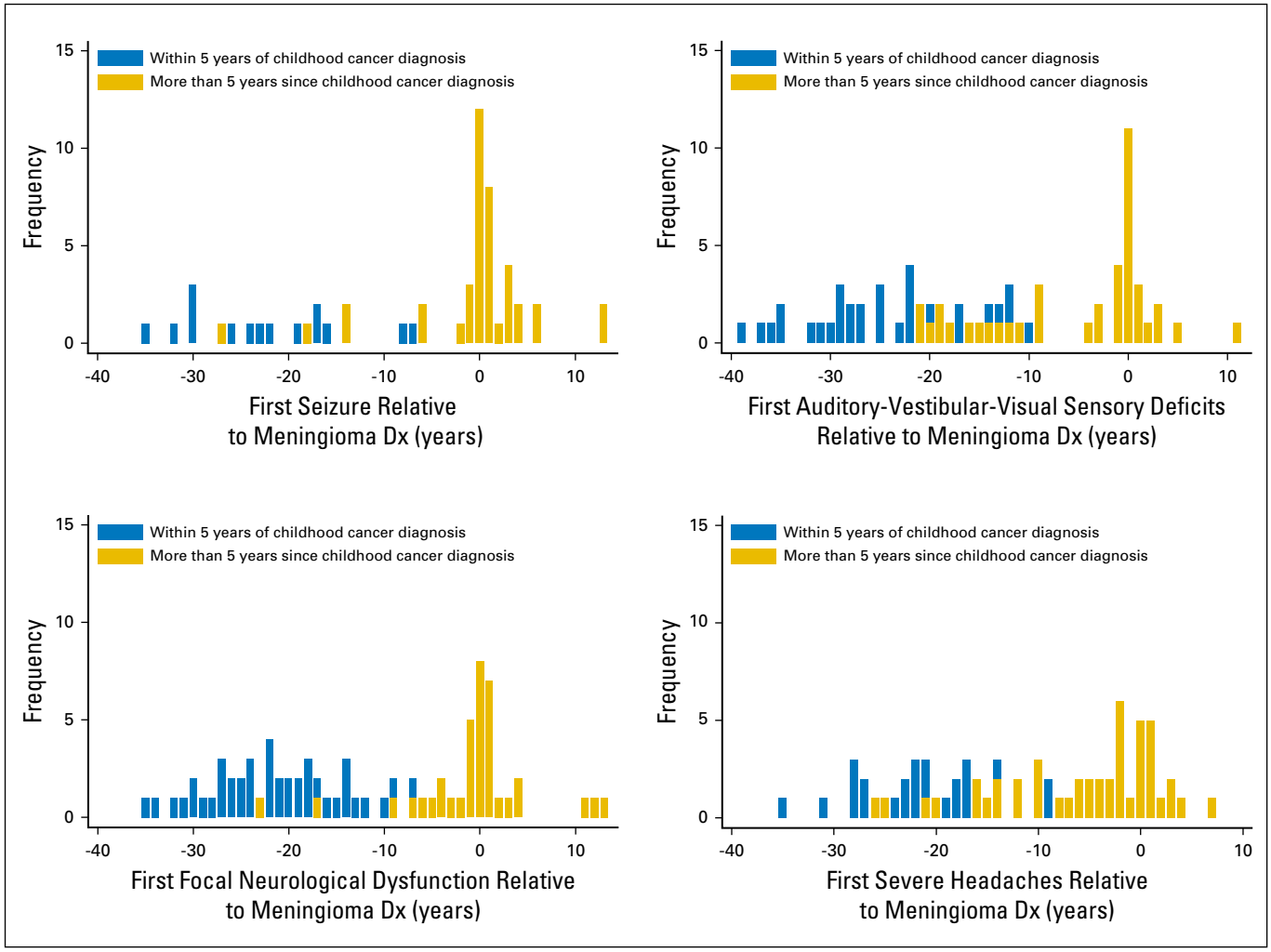

Fig 2. Onset of diagnosis of neurologic morbidity compared with onset of subsequent meningiomas among childhood cancer survivors exposed to cranial radiation. Dx, diagnosis.

The findings of this study are consistent with those of previous studies that identified an association between risk of meningiomas and increasing CRT dose.[1,5,11] Unlike those studies, however, this study identified an association between younger ages at primary cancer diagnosis and risk of subsequent meningioma. Furthermore, to our knowledge, this is the first study to identify an increased risk of meningiomas among female cancer survivors exposed to CRT, consistent with an increased risk of de novo meningiomas observed among women in the general population.[23] This observation was not seen in a previous report by Neglia et al[11] from the CCSS that examined CRT-associated meningiomas; indeed, this previous CCSS study suggested that men had an increased excess relative risk per 1 Gy CRT exposure. This study, with larger numbers of subjects and longer follow-up than was previously available, found that women had a significantly higher risk of subsequent meningiomas than did men after adjusting for the dose of CRT.

Screening asymptomatic cancer survivors exposed to CRT would likely lead to the detection of even more meningiomas than were found in this study. Four prospective studies, examining a total of 277 childhood leukemia survivors exposed to CRT, have assessed the impact of screening on ascertainment of asymptomatic meningiomas.[14-16,24] With median intervals of 16 to 27.9 years after exposure to CRT, 47 subjects (17%) were found to have meningiomas. This rate is considerably higher than the 5.6% cumulative incidence of subsequent meningiomas observed in this study, possibly because the patients participated in a screening study as opposed to waiting until the onset of symptoms that led to a meningioma diagnosis. This difference likely reflects the number of asymptomatic meningiomas that could be identified by periodic screening, perhaps resulting in a reduction in neurologic morbidity among cancer survivors exposed to CRT.

In this study, the OS rate at 72 months after the diagnosis of a subsequent meningioma was 87%. A report from the British CCSS examined a similar cohort of 132 participants who were diagnosed with subsequent meningiomas and found a 5-year survival rate of 84.3%.[13] Most of the deaths in the British CCSS were as a result of the meningioma. In contrast, the causes of death we observed in this study were variable, including the subsequent meningioma, progression of the

Table 3. Multivariate Analysis of Neurologic Morbidities Among Survivors Treated with CRT

Characteristic	Seizure (n = 3,729)				Auditory-Vestibular-Visual Sensory Deficits (n = 3,297)				Focal Neurologic Dysfunction (n = 3,164)				Severe Headache (n = 3,351)			
	Event No.	HR	95% CI	*P*	Event No.	HR	95% CI	*P*	Event No.	HR	95% CI	*P*	Event No.	HR	95% CI	*P*
Subsequent meningioma*																
Yes	41	10.0	(7.0 to 15.3)	< .001	41	2.3	(1.3 to 4.0)	.005	37	4.9	(3.2 to 7.5)	< .001	46	3.2	(1.9 to 5.4)	< .001
No	294	1.0	—		428	1.0	—		398	1.0	—		598	1.0	—	
Sex																
Female	162	1.1	(0.9 to 1.4)	.373	216	1.0	(0.8 to 1.2)	.698	213	1.2	(0.9 to 1.4)	.114	411	2.4	(2.1 to 2.8)	< .001
Male	176	1.0	—		253	1.0	—		222	1.0	—		233	1.0	—	
CRT exposure, Gy																
≥ 30	179	3.4	(2.4 to 4.6)	< .001	208	3.4	(2.7 to 4.3)	< .001	162	2.3	(1.8 to 3.0)	< .001	151	0.7	(0.6 to 0.9)	.002
20-29.9	104	1.4	(1.01 to 2.0)	.039	166	1.1	(0.8 to 1.4)	.416	177	1.2	(0.9 to 1.6)	.110	276	0.9	(0.8 to 1.1)	.283
1-5-19.9	52	1.0	—		95	1.0	—		96	1.0	—		217	1.0	—	

Abbreviation: CRT, cranial radiotherapy.
*Meningioma was treated as a time-dependent covariate in a Cox regression model. Numbers included in each neurologic morbidity outcome varied on the basis of complete data.

primary cancer, secondary anaplastic astrocytomas, and others. Although most late-mortality events in this study were not directly a result of the meningioma, a meningioma diagnosis may serve as a sentinel event associated with a future risk of premature death by other mechanisms besides the meningioma.

When interpreting the findings of this study, several limitations should be considered. First, although subsequent meningiomas were confirmed by pathology reports or other medical records, the occurrence and timing of neurologic sequelae were obtained by self-report, and the true incidence of neurologic sequelae may have been under-reported. Second, the study design is limited by the integration of calendar dates from pathology reports or other medical records to determine participants' age at subsequent meningiomas diagnosis with the participants' self-reported chronological age at first onset of neurologic sequelae. This methodology is able to identify up to a 6-month temporal relationship between the timing of meningioma diagnosis and the onset of neurologic sequelae. Third, the onset of neurologic morbidity occurred within 6 months before or after the meningioma diagnosis, and this study was not able to determine whether the meningioma-associated morbidity was a result of the subsequent meningioma or its treatment. Finally, this is a young cohort with a relatively small number of meningiomas compared with the total number of survivors with exposure to CRT. Results may change as the cohort ages and more meningiomas develop.

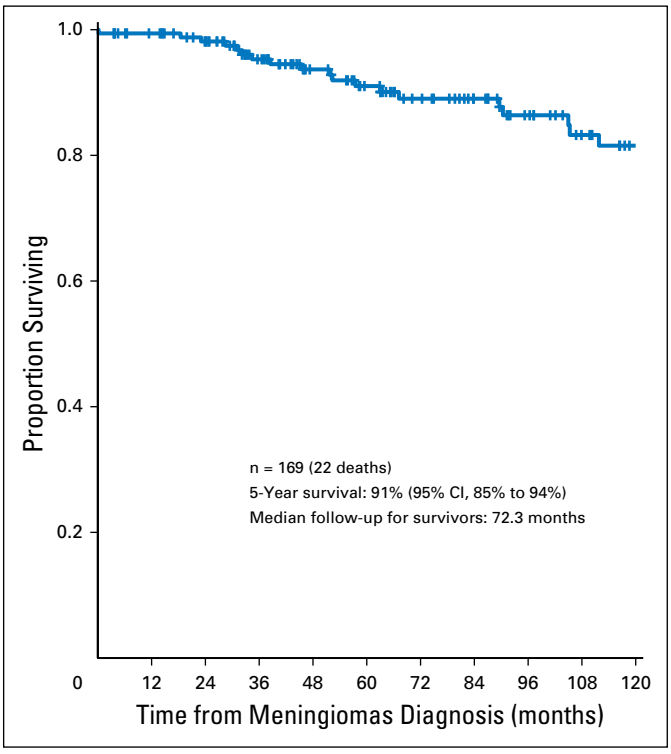

Fig 3. Cumulative survival after the diagnosis of a meningioma among 5-year survivors of childhood cancer.

In conclusion, childhood cancer survivors exposed to CRT have an increased rate of subsequent meningiomas. Survivors who are female, were diagnosed with cancer at a younger age, or were exposed to higher doses of CRT seem to be at especially high risk. Importantly, this study demonstrates that survivors with subsequent meningiomas have high rates of neurologic sequelae and increased mortality. Although it has not yet been proven to reduce morbidity or mortality, surveillance of cancer survivors who have been exposed to CRT will identify asymptomatic meningiomas[14-16,24] and will possibly allow for a reduction in neurologic morbidity. Further work is necessary to understand the cause of meningiomas after cancer therapy and to test the harms and benefits associated with noninvasive surveillance strategies, which may lead to a reduction in meningioma-associated morbidity and mortality.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: Daniel C. Bowers, Chaya S. Moskowitz, Joanne F. Chou, Leslie L. Robison, Kevin C. Oeffinger
Provision of study materials or patients: Joseph P. Neglia
Collection and assembly of data: Daniel C. Bowers, Chaya S. Moskowitz, Joanne F. Chou, Wendy M. Leisenring, Kevin C. Oeffinger
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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Support

Supported by Grants No. CA55727 and No. CA21765 (Cancer Center Support Grant) from the National Cancer Institute, and by the American Lebanese-Syrian Associated Charities. Additional support by Grant No. CA008748 from the National Cancer Institute.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Morbidity and Mortality Associated With Meningioma After Cranial Radiotherapy: A Report From The Childhood Cancer Survivor Study

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

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Consulting or Advisory Role: BioClinica

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