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ORIGINAL ARTICLE

Comprehensive assessment of sexual function in male survivors of childhood cancer: A report from the Childhood Cancer Survivor Study

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Abstract

Background: Assessment of sexual dysfunction among adult male survivors of childhood cancer has primarily been limited to erectile dysfunction. This study aimed to characterize sexual functioning more comprehensively among a large population of male survivors of childhood cancer.

Methods: Male survivors (N = 1595, 22.0–59.4 years, median age, 37.8 years) and siblings (N = 269, 21.5–60.8 years, median age, 38.9 years) from the Childhood Cancer Survivor Study completed the Sexual Functioning Questionnaire (SFQ) to assess interest, desire, arousal, satisfaction, activity, orgasm, masturbation, relationship, and problems. Poor sexual functioning was defined as SFQ Total scores >2 standard deviations below siblings' mean. Multivariable logistic regression identified risk factors for poor sexual function.

Results: Survivors (8.3%) were more likely to report poor sexual functioning as compared to siblings (4.9%, odds ratio [OR], 1.9; 95% confidence interval [CI], 1.1–3.4) and reported lower SFQ total scores (p < .001) and lower means on seven subscales. Poor sexual functioning among survivors was associated with older age (40–49 years: OR, 3.81; 95% CI, 1.78–8.18; 50–59 years: OR, 6.45; 95% CI, 2.28–18.30), not being married (OR, 4.39; 95% CI, 2.66–7.26), lower education (OR, 3.07; 95% CI, 1.32–7.14), learning/memory problems (OR, 1.83; 95% CI, 1.02–3.27), and high-dose cranial (≥40 Gy: OR, 3.45; 95% CI, 1.58–7.51) or high-dose testicular (≥10 Gy: OR, 4.16; 95% CI, 1.66–10.39) radiation.

Conclusions: Adult male survivors report poor sexual functioning at twice the rate expected before age 60 years. High-dose cranial or testicular radiation, as well as social and cognitive factors, contributes to risk. Improved awareness of sexual

dysfunction prevalence and risk factors in male childhood cancer survivors can help clinicians better assess and treat those at highest risk.

KEYWORDS
childhood cancer, health knowledge, sexual functioning, survivors

INTRODUCTION

In the modern era, >85% of children will survive their primary cancer, resulting in what is now more than 500,000 survivors of childhood cancer alive in the United States.[1] In recent years, the impact of childhood cancer on adult male survivors' sexual health has been investigated,[2–6] and clinical practice guidelines have been established to assist long-term follow-up providers in identifying males who are at increased risk for physical sexual dysfunction (i.e., erectile and/or ejaculatory dysfunction).[7,8] Much of the sexual dysfunction research among male survivors has occurred in the context of assessing erectile dysfunction (ED). Previous research from the Childhood Cancer Survivor Study (CCSS) and the St. Jude Life cohorts has found prevalence of ED among survivors ranging from 12% to 29%.[2,4] Yet sexual functioning is multidimensional in nature, and studies have demonstrated that male survivors of childhood cancer often report symptoms of sexual dysfunction beyond ED, including problems with enjoyment, arousal, satisfaction, and fear of sex.[3,9–12]

Problems with sexual function, including dissatisfaction, can negatively impact quality of life. Young adult survivors of childhood cancer with sexual dysfunction have reported poorer physical functioning, mental health, and life satisfaction and greater distress, depression, and anxiety.[13,14] Although sexual dysfunction in survivors of childhood cancer is likely amenable to treatment, further research is needed to inform multidisciplinary interventions tailored to this population.[11,15] A biopsychosocial approach is necessary to better understand sexual function, which is influenced by biological factors, including hormones and physical function; psychological factors, including cognitive and mental health; and social factors, including relationships and social functioning.[6,11] Thus, male survivors' sexual functioning is not yet well understood, and more research is needed that investigates the various dimensions of sexual functioning among male survivors.

To address this research gap, the objective of our investigation was to characterize sexual function problems in a large population of adult male survivors of childhood cancers. More specifically, we sought to determine the prevalence of poor sexual functioning among survivors as compared to siblings and to evaluate the demographic, psychosocial, and treatment factors associated with survivor reports of poor sexual functioning. We hypothesized male survivors of childhood cancer would experience higher rates of poor sexual functioning as compared to sibling controls. We also hypothesized male survivors would report similar levels of sexual interest but lower levels of functioning in other domains (e.g., arousal, satisfaction, etc.) as compared to controls. Because older age has been consistently associated with poorer sexual functioning among male survivors of childhood cancer,[3,13,14] we believed that aging would negatively impact survivors' sexual functioning. After controlling for this important factor, we hypothesized that poor sexual functioning would be associated with multiple other factors, including cancer type and/or subsequent treatment, chronic medical conditions, and psychosocial functioning.

MATERIALS AND METHODS

CCSS

Male participants were recruited from the CCSS cohort of ≥5-year survivors of childhood cancer and siblings from 26 institutions in the United States and Canada. Details of the CCSS study design and cohort have been previously published.[16,17] Participants' self-reported demographic characteristics, history of cardiac events, and problems with learning or memory (e.g., "Have you ever been told by a physician or other health care professional that you have, or have had, problems with learning or memory?") were obtained from the CCSS baseline and follow-up questionnaires. Cardiac condition severity scoring was based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE, version 4.03) as previously described.[18]

Men's Health Questionnaire

The Men's Health Questionnaire (MHQ) was an ancillary study to CCSS, developed to obtain information about male reproductive health and perceptions of risk for male health late effects related to childhood cancer treatment. Survivors with male sex assigned at birth who were ≥18 years old when they participated in CCSS' Follow-up 4 Questionnaire (2007–2008, $N = 4000$) were asked to consider completing a separate survey to "better understand fertility and sexual function in males." Overall, $N = 2961$ survivors agreed to receive the MHQ (Figure S1). As part of the MHQ, participants completed the Sexual Functioning Questionnaire (SFQ). The SFQ was developed and validated to assess overall sexual functioning among cancer survivors, including adult survivors of childhood cancer[19] The SFQ consists of nine multi-item subscales assessing physical and psychosocial domains, including interest, desire, arousal, orgasm, satisfaction, activity, relationship, masturbation, and male sexual problems (difficulty getting an erection, lack

of sexual interest or desire, losing an erection during sexual activity, delayed ejaculation, anxiety about sexual performance, unable to achieve orgasm, and/or pain during penetration or intercourse). The SFQ subscale items are averaged to calculate the SFQ total mean score, with higher scores representing better functioning. Among a population of adult male survivors of cancer and/or bone marrow transplants, the SFQ has demonstrated strong psychometric properties.[19] Additional self-reported data collected on the MHQ included dichotomous "Yes" or "No" responses to a history of depression, obsessive-compulsive disorder, other major psychiatric illnesses (i.e., schizophrenia, paranoia), spinal cord injury, prostate disease, and pelvic surgery. The complete MHQ can be found at https://ccss.stjude.org/content/dam/en_US/shared/ccss/documents/survey/survey-mens-health-2007.pdf.

Medical record abstraction for cancer treatment exposures

Clinical data for these analyses (cancer diagnosis, chemotherapy exposures, radiation treatments, and surgeries) were previously abstracted from participants' treating institution medical records. Estimates of organ- and tissue-absorbed radiation doses were calculated using previously reported methods.[17,20] Cranial radiation exposure was dichotomized as low (>0 to <40 Gy) versus high (≥40 Gy), whereas testicular radiation was dichotomized as low (>0 to <10 Gy) versus high (≥10 Gy).

Statistical analyses

Participants who did not complete the SFQ on the MHQ ($N = 27$) were excluded from analyses. Participant characteristics and outcome variables were summarized with descriptive statistics. Survivor SFQ Total and subscale score means were compared to sibling controls using generalized linear models with robust variances to account for intrafamily correlations. Participants with SFQ Total mean scores more than two standard deviations below the siblings' population mean were categorized as reporting poor sexual functioning, a threshold commonly used to identify significantly impaired functioning by capturing those at the lower end of the distribution where meaningful deficits are most likely.[21] Logistic regression evaluated factors associated with survivors' self-reported poor sexual functioning. Factors showing a univariable association with poor sexual functioning at the $p < .10$ level were further assessed in multivariable models. The final multivariable model included treatment exposures, plus demographic and medical characteristics that demonstrated statistically significant associations with poor sexual functioning or whose omission would impact other estimates from the model by more than 10%. A separate analysis was conducted to evaluate cancer diagnosis type as a risk factor for poor sexual functioning among male survivors. p values less than .05 are considered statistically significant.

RESULTS

Participants and nonparticipants

The MHQ was completed and returned by 1622 survivors (55.1% response rate; Figure S1). Demographics and treatment characteristics for participants are presented in Table 1. At the time of survey completion, survivors were a median of 37.8 years of age (range: 22.0–59.4 years) and 28.4 years from diagnosis (range: 21.4–39.2 years), whereas siblings were a median age of 38.9 years (range: 21.5–60.8 years). Most male survivors in our population identified as non-Hispanic White (93.4%), received at least some college education (84.9%), were working full time (81.7%), and were married or living as married (65.3%). Sibling participants were slightly older than survivors ($p < .01$), more likely to identify as non-Hispanic White ($p = .04$), and more likely to be employed full-time ($p = .02$). When compared to nonparticipants, survivors who completed the MHQ were slightly older at diagnosis and time of survey, were more likely to be White, reported higher income and level of education, were more likely to have fathered a child, and have married or lived as married (Table S1).

Sexual functioning in survivors versus siblings

Almost all survivors (92.9%) and siblings (97.4%) reported engaging in sexual activity either alone or with a partner in the past year. Compared to 4.9% (95% confidence interval [CI], 2.6%–8.2%) of siblings, 8.3% (95% CI, 7.0%–9.7%) of survivors reported poor sexual functioning. After adjusting for age at MHQ, survivors were almost twice as likely to report poor sexual functioning as compared to siblings (odds ratio [OR], 1.9; 95% CI, 1.1–3.4). On the SFQ subscales (Table 2), survivors most frequently reported sexual problems (12.8%), low satisfaction (12.0%), and low desire (9.9%). As compared to siblings, survivors also reported significantly lower SFQ Total mean scores ($p < .001$) and lower means on seven of the SFQ subscales, including interest ($p = .022$), arousal ($p = .01$), orgasm ($p < .001$), satisfaction ($p < .001$), activity ($p = .003$), masturbation ($p = .005$), and problems ($p < .001$) (Table 2).

Factors associated with poor sexual functioning among male survivors

Male survivors were more likely to report poor sexual functioning if they were older at the time of survey (Table 3). Specifically, survivors 40–49 years old (OR, 3.81; 95% CI, 1.78–8.18) and 50–59 years old (OR, 6.45; 95% CI, 2.28–18.30) were more likely to report poor sexual functioning as compared to survivors 20–29 years old. Male survivors were more likely to report poor sexual functioning if they were not married or living as married (OR, 4.39; 95% CI, 2.66–7.26) or did not attend college (OR, 3.07; 95% CI, 1.32–7.14, referent: post-graduate education). Survivors who were employed full-time

TABLE 1 Demographic and treatment characteristics of adult male survivors of childhood cancer and sibling comparison population.[a]

	Survivors		Siblings		
Characteristics	***N* = 1595**	**%**	***N* = 269**	**%**	***p***
Age at MHQ, years					<.01
20–29	266	16.68	43	15.99	
30–39	695	43.57	107	39.78	
40–49	551	34.55	89	33.09	
50–59	83	5.20	30	11.15	
Race/ethnicity					.04
White, non-Hispanic	1417	93.35	252	97.30	
Black, non-Hispanic	30	1.98	0	0.00	
Hispanic	44	2.90	4	1.54	
Other	27	1.78	3	1.16	
Marital status					.15
Not married/living as married	550	34.66	81	30.11	
Married/living as married	1037	65.34	188	69.89	
Education					.48
Did not attend college	240	15.05	43	15.99	
Some college	378	23.70	54	20.07	
College graduate	652	40.88	109	40.52	
Post graduate level	325	20.38	63	23.42	
Employed ≥30 h/week					.02
Yes	1301	81.72	236	87.73	
No	291	18.28	33	12.27	
Age at primary cancer diagnosis, years					
≤4	544	34.11			
5–9	353	22.13			
10–14	371	23.26			
15–21	327	20.50			
Diagnosis type					
Leukemia	527	33.04			
CNS tumor	134	8.40			
Hodgkin lymphoma	258	16.18			
Non-Hodgkin lymphoma	173	10.85			
Wilms tumor	129	8.09			
Neuroblastoma	79	4.95			
Soft tissue sarcoma	143	8.97			
Bone cancer	152	9.53			
Subsequent malignant neoplasm					
Yes	85	5.33			
No	1510	94.67			

TABLE 1 (Continued)

Characteristics	Survivors N = 1595	%	Siblings N = 269	%	p
Recurrence of primary neoplasm					
Yes	189	11.85			
No	1406	88.15			
Cranial radiation, Gy					
None	496	33.40			
>0 to <40	885	59.60			
≥40	104	7.00			
Testicular radiation, Gy					
None	497	33.79			
>0 to <10	905	61.53			
≥10.0	69	4.70			
Cyclophosphamide equivalent dose (mg/m^2)					
0	666	47.67			
≥1 to <4000	170	12.17			
≥4000 to <8000	169	12.10			
≥8000 to <12,000	150	10.74			
≥12,000 to <16,000	97	6.94			
≥16,000 to <20,000	70	5.01			
≥20,000	75	5.37			
Surgery on spinal cord or sympathetic nerves					
Yes	42	2.78			
No	1470	97.22			
History of pelvic surgery					
Yes	39	2.53			
No	1502	97.47			
History of spinal injury					
Yes	75	4.93			
No	1446	95.07			
History of prostate disease					
Yes	35	2.30			
No	1490	97.70			
History of depression					
Yes	227	14.51			
No	1337	85.49			
History of grade 3+ cardiac condition					
Yes	125	7.84			
No	1470	92.16			

(Continues)

TABLE 1 (Continued)

Characteristics	Survivors N = 1595	%	Siblings N = 269	%	p
Problems with learning or memory					
Yes	215	13.74			
No	1350	86.26			

Abbreviations: CNS, central nervous system; MHQ, Men's Health Questionnaire.
[a]Percentages provided for those with known demographic or treatment status.

TABLE 2 Sexual functioning in male survivors versus siblings.

SFQ scale	Survivors (N = 1595) No.	% <2 SD below sibling M	M	95% CI	Siblings (N = 269) No.	M	95% CI	β coefficient[a]	p
SFQ Total mean score	1560	8.27	3.52	3.47–3.56	265	3.72	3.62–3.81	−0.21	<.001
Interest	1567	4.40	3.59	3.53–3.66	266	3.77	3.61–3.93	−0.20	.022
Desire	1565	9.93	3.83	3.75–3.91	269	4.01	3.84–4.18	−0.18	.06
Arousal	1556	5.53	2.95	2.88–3.03	264	3.18	3.00–3.35	−0.24	.01
Orgasm	1580	9.11	3.96	3.90–4.02	265	4.22	4.10–4.33	−0.25	<.001
Satisfaction	1593	11.99	3.87	3.80–3.93	268	4.16	4.04–4.29	−0.29	<.001
Activity	1542	0	2.43	2.36–2.51	265	2.71	2.55–2.88	−0.27	.003
Relationship	1263	6.18	4.00	3.94–4.05	229	4.01	3.90–4.13	−0.04	.51
Masturbation	1561	0	2.55	2.46–2.64	266	2.80	2.59–3.01	−0.31	.005
Male sexual problems[b]	1551	12.83	4.66	4.63–4.69	261	4.78	4.73–4.82	−0.14	<.001

Abbreviations: CI, confidence interval; M, mean; SD, standard deviation; SFQ, Sexual Functioning Questionnaire.
[a]Mean difference for survivors compared with siblings, adjusted for age at study and marital status.
[b]Higher score indicates fewer or less frequent sexual problems.

(OR, 0.46; 95% CI, 0.28–0.77) were less likely to report poor sexual functioning than those who were unemployed or working part-time. Survivors who received high-dose cranial (≥40 Gy: OR, 3.45; 95% CI, 1.58–7.51) or high-dose testicular radiation (≥10 Gy: OR, 4.16; 95% CI, 1.66–10.39) were more likely to report poor sexual functioning compared to those treated with no radiation. Survivors with a history of learning or memory problems (OR, 1.83; 95% CI, 1.02–3.27) were also more likely to report poor sexual functioning. History of subsequent malignant neoplasm or relapsed primary disease, prostate disease, depression, and other major psychiatric disorders were significantly associated with poor sexual functioning in univariate analyses; however, none of these were significant in the multivariable model. Age at primary diagnosis, cyclophosphamide equivalent dose, surgery on spinal cord or sympathetic nerves, pelvic surgery, spinal injury, and history of cardiac condition were not associated with poor sexual functioning.

In a secondary model, we sought to evaluate cancer diagnosis as a risk factor for poor sexual functioning after controlling for age at MHQ (Table 4). As compared to survivors of acute lymphoblastic leukemia, male survivors of medulloblastoma (OR, 5.64; 95% CI, 2.23–14.25) and other central nervous system (CNS) tumors (OR, 4.03; 95% CI, 1.54–10.53) were more likely to report poor sexual functioning, whereas male survivors of Hodgkin lymphoma (OR, 0.36; 95% CI, 0.18–0.73) and soft tissue sarcoma (OR, 0.30; 95% CI, 0.11–0.79) were less likely to report poor sexual functioning.

DISCUSSION

A significant proportion of male survivors of childhood cancer report poor overall sexual function at nearly twice the rate observed among sibling comparisons in our study. Our findings broaden the understanding of male sexual functioning in this population by integrating psychosexual dimensions, highlighting low satisfaction and diminished sexual desire as commonly reported challenges. Notably, despite the relatively young age of the cohort, with 95% of participants under 50 years of age, survivors reported higher rates of sexual problems compared with siblings across seven of nine measured domains of sexual function. By using siblings as a normative

TABLE 3 Demographic and treatment factors associated with poor overall sexual functioning among male survivors.

Factors	Categories	Adjusted OR (95% CI)	*p*
Age at MHQ	20–29 years	1.00 (referent)	—
	30–39 years	1.72 (0.82–3.62)	.15
	40–49 years	3.81 (1.78–8.18)	<.01
	50–59 years	6.45 (2.28–18.30)	<.01
Marital status	Married/living as married	1.00 (referent)	—
	Not married/living as married	4.39 (2.66–7.26)	<.0001
Education	Post-graduate level	1.00 (referent)	—
	College graduate	2.07 (0.94–4.55)	.07
	Some college	2.17 (0.94–5.00)	.07
	Did not attend college	3.07 (1.32–7.14)	<.01
Employed ≥30 hours per week	Yes	0.46 (0.28–0.77)	<.01
	No	1.00 (referent)	—
Radiation treatment[a]	High dose cranial only	3.45 (1.58–7.51)	<.01
	Low cranial, low testicular	1.27 (0.71–2.28)	.42
	Low cranial, high testicular	4.16 (1.66–10.39)	<.01
	No radiation	1.00 (referent)	—
SMN or recurrence	Yes	1.60 (0.91–2.79)	.10
	No	1.00 (referent)	—
History of prostate disease	Yes	2.24 (0.67–7.56)	.19
	No	1.00 (referent)	—
History of mental health disorder	Depression only	1.39 (0.75–2.57)	.30
	Depression and OCD or major psychiatric disorder	1.51 (0.40–5.75)	.54
	Other major psychiatric disorder	2.01 (0.31–13.19)	.47
	No history of depression, OCD, or other major psychiatric disorder	1.00 (referent)	—
History of learning or memory problems	Yes	1.83 (1.02–3.27)	.04
	No	1.00 (referent)	—

Abbreviations: CI, confidence interval; MHQ, Men's Health Questionnaire; OCD, Obsessive Compulsive Disorder; OR, odds ratio; SMN, subsequent malignant neoplasm.

[a]Cranial radiation (low >0 to <40 Gy, high ≥40 Gy); testicular radiation (low >0 to <10 Gy, high ≥10.0 Gy).

reference group, our study enhances clinical relevance by partially accounting for shared environmental factors, allowing for a more precise evaluation of sexual dysfunction attributable to childhood cancer and its treatment. These results support our hypothesis that although the desire for sexual activity is comparable between survivors and siblings, male survivors of childhood cancer are disproportionately affected by sexual dysfunction during their early adulthood and middle age years.

Previous studies have established that survivors have an increased risk for erectile dysfunction compared with siblings or healthy controls.[2,3,10,12] Our findings advance this work by identifying that erectile function is only one facet of male sexual functioning, as our findings extend the understanding of the relevant psychosexual domains that are negatively impacted among survivors (e.g., interest, arousal, orgasm, satisfaction) as compared to controls. Compared with siblings, survivors reported more frequent sexual functioning problems that have the potential to thwart sexual activity, including difficulty with erection, delayed ejaculation, inability to achieve orgasm, or anxiety about sexual performance. Our multivariable analyses found that in addition to age and radiation, psychosocial and cognitive factors (e.g., education, employment, and problems with learning/memory) were associated with a higher likelihood of poorer sexual function, resulting in modified risk profiles compared with prior research in the CCSS population. Overall, our findings advance what is known regarding sexual function among male survivors of childhood cancer by assessing multidimensional aspects of sexual function among a population of sexually active survivors (either alone or with a partner).

TABLE 4 Cancer diagnosis and poor sexual functioning among male survivors.

Cancer diagnosis group	Adjusted OR[a] (95% CI)	*p*
Acute lymphoblastic leukemia	1.00 (referent)	—
Acute myeloid leukemia	1.79 (0.50, 6.42)	.40
Other leukemia	1.83 (0.39, 8.61)	.44
Astrocytomas	1.86 (0.95, 3.64)	.07
Medulloblastoma, PNET	5.64 (2.23, 14.25)	<.01
Other CNS tumors	4.03 (1.54, 10.53)	<.01
Hodgkin lymphoma	0.36 (0.18, 0.73)	<.01
Non-Hodgkin lymphoma	0.64 (0.32, 1.26)	.20
Kidney tumors	0.59 (0.24, 1.44)	.25
Neuroblastoma	0.70 (0.24, 2.04)	.51
Soft tissue sarcoma	0.30 (0.11, 0.79)	.02
Ewing sarcoma	1.24 (0.49, 3.15)	.65
Osteosarcoma or other bone tumor	0.47 (0.19, 1.13)	.09

Abbreviations: CNS, central nervous system; OR, odds ratio; PNET, primitive neuroectodermal tumor.

[a]Adjusted for survivor age at Men's Health Questionnaire.

We found that cranial and testicular radiation is associated with poor sexual functioning when given in high doses (≥40 Gy and ≥10 Gy, respectively). Importantly, we did not find a significant association with some treatment exposures outlined in national and international screening guidelines for physical sexual dysfunction after childhood cancer treatment.[8,22] Specifically, poor sexual function was not associated with the cyclophosphamide-equivalent dose, nor was history of prostate surgery, surgery to spinal cord/nerves, or pelvic surgery. We also did not find that chronic medical conditions (e.g., cardiac or prostate disease) or mental health disorders were associated with poor sexual functioning in multivariable analyses. Consideration of the additive effect of age and these treatment-related risk factors should be incorporated in future work. Additionally, broad dimensions of depression and anxiety may be less sensitive to screening in survivors with sexual functioning problems, whereas screening for body image and relationship satisfaction could be more sensitive measures in identifying men with sexual health problems, as these have been found to be relevant in other studies of survivors.[11,12,14,23] We did, however, identify several social risk and resilience factors, with men who were unmarried or not having attended college being more likely to experience poor sexual function and men who were employed full-time less likely to experience poor sexual function. In relation to cognitive dysfunction, having a history of learning or memory problems also increased risk for poor sexual function. In European population-based studies of survivors, problems with sexual functioning and lower sexual satisfaction were similarly related to social factors (e.g., lower education, not being in a relationship, and poorer body perception).[12,23] Collectively, these findings underscore how biopsychosocial factors influence male survivors' sexual functioning and highlight the need for integrative approaches to screening and intervention to address these interrelated dimensions comprehensively.

Given the impact of cranial radiation and psychosocial functioning on sexual function, CNS tumor survivors are particularly at greater risk for poor sexual function,[24] which we observed in comparison to leukemia survivors. Compared with survivors of other childhood cancers, survivors of CNS tumors more frequently report problems with sexual arousal, satisfaction, and fewer sexual partners.[24] Low testosterone can be associated with erectile dysfunction in survivors of childhood cancer, which could be a driver of poor sexual function found in survivors of CNS tumors who experience hypogonadism after cranial radiation.[4] Survivors of brain tumors are also less likely to marry, earn a college degree, and more likely to be unemployed compared with control populations.[25–27] Cranial radiation is associated with long-term cognitive impairments, including problems with attention/memory and a lack of social independence.[28] Although cranial radiation may be an important driver of poor sexual function, we found that social function was associated with sexual dysfunction independent of radiation therapy. The relationships between poor sexual function and social factors may be bidirectional. For example, poor sexual function could either result from or hinder CNS survivors from forming committed romantic relationships. Survivors of Hodgkin lymphoma or soft tissue sarcoma (two diagnoses that do not typically receive cranial irradiation or experience learning and memory problems) appear to be at lower risk for sexual problems relative to survivors of leukemia. Cranial radiation is an established risk factor for learning and memory problems, whereas deficits in learning and memory are associated with social impairments among childhood cancer survivors. The ability to learn about and cognitively process social cues are essential for attracting, establishing, and maintaining healthy sexual relationships. When one considers the increased risk for poor sexual functioning experienced by CNS tumor survivors, as observed in our study, an elevated profile for poor sexual functioning emerges and clarifies additional targets for screening and intervention.

These findings should be considered in the context of study limitations. Despite a large population, only 74% of male survivors within the CCSS cohort opted to receive the Male Health Questionnaire, and only 56% of those returned a completed survey. Survivors who completed the survey were slightly older and more likely to be married or lived as married compared with nonresponders. Non-White race/ethnicity has been associated with erectile dysfunction in previous cancer survivor research[4]; however, we were unable to explore these relationships further as the majority of survivors in our population were non-Hispanic White. These factors may have contributed to an underestimate of poor sexual function among survivors. Our study may have lacked sufficient power to detect sexual dysfunction among survivors with a history of prostate surgery, spinal cord or nerve surgery, or pelvic surgery due to the small sample sizes within these subgroups. Additionally, survivors who underwent these procedures may have received sexual health support as part of their rehabilitation, potentially mitigating dysfunction

and contributing to the absence of significant findings. Future research should explore the potential impact of total body irradiation on sexual function in childhood cancer survivors, as its effects may differ from those of testicular radiation alone. Finally, hypogonadism, a known risk factor for sexual dysfunction, was not explored in this study.

Continued research assessing the multidimensional aspects of sexual function is needed to direct clinical guidelines and intervention development. Given the relatively young age of survivors in this study, future studies can examine if sexual problems increase with age as a function of normative andropause or if this is exacerbated by other late effects associated with cancer treatment. Further research is needed to better characterize sexual dysfunction in adolescent- and young adult-aged survivors who are closer to treatment. Finally, integrative treatments are needed for survivors that address any identified physiological dysfunction and psychosocial needs.

Findings from this study reinforce the need for a biopsychosocial approach to screening and intervention to support sexual function. Survivors would benefit from routine screening for sexual function as part of survivorship care. Survivor care clinicians may consider using existing patient-reported outcomes measures to assess sexual function,[29] although the clinical utility and strategies for implementation of screening within the clinical environment are not yet established. Addressing sexual function problems often requires an integrative approach, engaging subspecialists such as urology, psychology, and sex therapists. Developing a referral network of interdisciplinary providers who can diagnose and intervene concerning sexual problems among survivors is important for oncology and survivorship clinicians. For survivors who endorse sexual functioning problems, interventions that incorporate a biopsychosocial approach to treatment are needed. In conclusion, the association between cancer treatment, psychosocial factors, and diminished sexual functioning among male survivors of childhood cancer underscores the critical need for comprehensive clinical screening and targeted interventions addressing the full spectrum of sexual health challenges in this population.

AUTHOR CONTRIBUTIONS

Jordan Gilleland Marchak: Conceptualization, writing–original draft, and writing–review and editing. **Kristy D. Seidel**: Data curation, formal analysis, methodology, software, and writing–review and editing. **Brooke O. Cherven**: Writing-reviewing and editing. **James L. Klosky**: Writing–reviewing and editing. **Chad W. M. Ritenour**: Conceptualization and writing–review and editing. **Wendy M. Leisenring**: Data curation, formal analysis, methodology, software, and writing–review and editing. **Charles A. Sklar**: Writing–review and editing. **Jennifer S. Ford**: Writing–review and editing. **Kevin R. Krull**: Writing–review and editing. **Leslie L. Robison**: Data curation, methodology, software, funding acquisition, investigation, and writing–review and editing. **Gregory T. Armstrong**: Data curation, methodology, software, funding acquisition, investigation, and writing–review and editing. **Lillian R. Meacham**: Conceptualization, funding acquisition, project administration, writing–review and editing, and supervision.

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CONFLICT OF INTEREST STATEMENT

Jordan Gilleland Marchak reports research funding from Pfizer Inc. Gregory T. Armstrong reports fees for professional activities from the National Institutes of Health. Wendy M. Leisenring reports grant and/or contract funding from the National Cancer Institute and the National Institutes of Health. The other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The Childhood Cancer Survivor Study (CCSS) is a US National Cancer Institute funded resource (U24 CA055727) to promote and facilitate research among long-term survivors of cancer diagnosed during childhood and adolescence. CCSS data are publicly available on dbGaP at https://www.ncbi.nlm.nih.gov/gap/ through its accession number phs001327.v2.p1.and on the St. Jude Survivorship Portal within the St. Jude Cloud at https://survivorship.stjude.cloud/. In addition, utilization of the CCSS data that leverages the expertise of CCSS Statistical and Survivorship research and resources will be considered case-by-case. For this utilization, a research Application of Intent followed by an Analysis Concept Proposal must be submitted for evaluation by the CCSS Publications Committee. Users interested in using this resource are encouraged to visit http://ccss.stjude.org.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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