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ONCOLOGY

Erectile Dysfunction in Male Survivors of Childhood Cancer—A Report From the Childhood Cancer Survivor Study

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ABSTRACT

Introduction: With survival rates higher than 80%, the number of survivors from pediatric cancer continues to increase. Late effects resulting from cancer and cancer therapy are being characterized, but little information exists on sexual health for men who have survived childhood cancer.

Aim: To assess erectile dysfunction (ED) in men who survived childhood and adolescent cancers and to identify potential risk factors for ED.

Methods: In total, 1,622 men and 271 eligible brothers in the Childhood Cancer Survivor Study cohort completed the Male Health Questionnaire, which provided information on sexual practices and sexual function. Combined with demographic, cancer, and treatment information from medical record abstraction, results of the Male Health Questionnaire were analyzed using multivariable modeling. The International Index of Erectile Function was used to identify ED in subjects.

Main Outcome Measure: International Index of Erectile Function.

Results: Survivors (mean age = 37.4 years, SD = 7.3 years) reported significantly lower sexual activity in the year before the survey than the brothers (mean age = 38.8 years, SD = 8.5 years) without cancer. ED was reported by 12.3% (95% CI = 10.4−14.3) of survivors and 4.2% (95% CI = 2.0−7.9) of brothers. Survivors showed significantly higher relative risk (RR) for ED (RR = 2.63, 95% CI = 1.40−4.97). In addition to older age, survivors who were exposed to higher-dose (≥10 Gy) testicular radiation (RR = 3.55, 95% CI = 1.53−8.24), had surgery on the spinal cord or nerves (RR = 2.87, 95% CI = 1.36−6.05), prostate surgery (RR = 6.56, 95% CI = 3.84−11.20), or pelvic surgery (RR = 2.28, 95% CI = 1.04−4.98) were at higher risk for ED.

Conclusion: Men who have survived childhood cancer have a greater than 2.6-fold increased risk for ED and certain cancer-specific treatments are associated with increased risk. Attention to sexual health, with its physical and emotional implications, and opportunities for early detection and intervention in these individuals could be important.

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Key Words: Cancer Survivorship; Sexual Dysfunction; Erectile Dysfunction; Pediatric Cancer

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INTRODUCTION

With advances in treatment for individuals diagnosed with cancer, survival rates for all ages continue to increase, and there is a growing focus on long-term health and quality of life in this population.[1,2] In consequence, there are increasing numbers of survivors of childhood cancer who face challenges as they age. More than 80% of those diagnosed with childhood cancer currently survive at least 5 years, and most recent estimates have reported nearly 400,000 survivors of childhood cancer in the United States at the start of 2012.[3] Despite significant advancement in knowledge on the health status of these survivors as they age,[4,5] relatively little information has been published on the sexual health of boys who have survived cancer as they transition to adulthood.

In general, men who have survived childhood cancers remain at risk for the sexual issues that all aging men face. However, the effects of a cancer diagnosis and treatment can add other risks and concerns.[6] We analyzed self-reported data from a large cohort of men who survived childhood cancer to better understand these issues. These data captured information related to sexual function and relationships, infertility, perceived risk from cancer and treatment, and overall health. In this particular report, we specifically address erectile dysfunction (ED) in this group, given the attention this subject has received in other populations and its relative lack in men who survived childhood cancer, recognizing that it is only one issue affecting these patients.

The Childhood Cancer Survivor Study (CCSS) cohort, consisting of more than 14,000 survivors who were diagnosed from 1970 through 1986,[7] was used to assess four specific areas: (i) the frequency and type of sexual activities reported by these men compared with adult sibling controls; (ii) the prevalence of ED using the International Index of Erectile Function (IIEF) in survivors compared with siblings; (iii) the effects of treatment and other sociodemographic, health, or cancer-related variables on erectile function (EF); and (iv) the frequency and types of therapies used to treat ED in surviving men compared with siblings.

METHODS

The CCSS is a retrospective cohort of 5-year survivors of childhood cancer from 26 participating institutions in the United States and Canada who were diagnosed from 1970 through 1986. Cancer diagnosis and treatment data were collected through medical record abstracts, and ongoing assessment of health and quality of life continues to be obtained through self-report in periodic surveys. Brothers of survivors were included as a comparison group. Details of the study design and cohort have been published.[7,8] The institutional review board at each institution approved the study; informed consent was obtained from all participants.

Primary diagnosis and detailed treatment data were collected using a structured medical record abstraction form. Cumulative alkylating agent exposure was calculated using cyclophosphamide equivalent dose.[9] The initial baseline questionnaire was administered beginning in 1994, with follow-up questionnaires through 2009.

At the fourth CCSS long-term follow-up questionnaire, men and siblings at least 18 years old (at time of completing the questionnaire) were asked if they would consider participating in a study "to better understand fertility and sexual function in males." In total, 2,961 survivors and 723 siblings (of the eligible 4,000 men and 1,097 brothers who completed the fourth follow-up questionnaire) expressed interest in completing this additional questionnaire. The Male Health Questionnaire (MHQ) was subsequently mailed in 2008 and 2009 to this group. The MHQ was created to obtain information about sexual experiences and practices, sexual function, infertility, testicular function, and perceptions of the impact of cancer diagnosis and treatment on sexual function in this cohort (questionnaires available at: https://ccss.stjude.org/documents/questionnaires/original-cohort-questionnaires.html).

Embedded within the MHQ was the previously validated IIEF.[10] The 15-question IIEF is divided into five domains: EF, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Each domain can be scored separately. An IIEF-EF domain score no higher than 25 was used as the definition of ED for this study.[11] The IIEF-EF domain items are designed to assess EF in men who have been sexually active within the past 4 weeks. IIEF-EF domain scores and the binary (yes vs no) outcome were computed only for subjects who were sexually active during the 4-week period before completing the questionnaire. All subjects were asked whether they had ever received treatment for ED. Subjects responding "yes" were asked to provide information about treatment type.

Other definitions were consistent with prior publications involving the CCSS cohort. Cardiac conditions followed the *Common Terminology Criteria for Adverse Events, Version 4.0* as recently reported for CCSS patients,[12] with grade 3 conditions considered severe or disabling and grade 4 conditions considered life-threatening. For physical activity, subjects who reported engaging in at least 30 minutes of moderate-intensity physical activity on at least 5 days per week or at least 20 minutes of vigorous physical activity on at least 3 days per week were classified as meeting the Centers for Disease Control and Prevention guidelines for physical activity that were in place at the time of the fourth follow-up questionnaire.[13] This is the same definition used in a previous report regarding physical activity in survivors of childhood cancer.[14]

Data Analysis

Data collected were tabulated for descriptive statistics, and statistical models were created to compare results between groups. Estimates of the relative risk (RR) and corresponding 95% CIs for ED and ED treatment were calculated using generalized linear modeling. A log-link model, rather than a logistic model, was chosen because ED was not rare in the study population and, hence, the log-link was more suitable for estimating RR. The model used a Poisson error distribution with