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N. J. Raghunathan

C. Benedict
Zucker School of Medicine at Hofstra/Northwell

B. Thom

D. N. Friedman

J. F. Kelvin

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Young Adult Female Cancer Survivors' Concerns About Future Children's Health and Genetic Risk

Nirupa Jaya Raghunathan, MD,[1,2] Catherine Benedict, PhD,[3] Bridgette Thom, MS,[1,2] Danielle Novetsky Friedman, MD, MS,[2,4] and Joanne Frankel Kelvin, MSN, RN, AOCN,[1,2]

As young adult female cancer survivors (aged 18–35) make family-building decisions, understanding the specific nature of their concerns is important. We evaluated survivors' concerns about potential health risks to future children including genetic susceptibility for cancer with an internet-based survey study ($N = 187$). Sixty-five percent reported concern about passing on a genetic cancer risk to their children, and scores did not vary regardless of association with cancer at high risk for genetic transmission. Genetic counseling and education about family-building options may be important to survivors concerned about health risks to offspring to support family-building decisions based on personalized medical information.

Keywords: family planning, genetic risk, fertility, late effects

Introduction

Concerns about cancer-related fertility and future family-building are multifaceted and can include fears about how a cancer diagnosis or treatment will affect future children's health.[1] This concern may be particularly relevant to young adult female cancer survivors (YAFCSs), currently aged 18–35 years who were treated at anytime in the past, as they are likely to have been diagnosed before starting or completing their desired childbearing.[2] As providers discuss options to preserve fertility before treatment through oocyte, embryo, or ovarian tissue cryopreservation, and provide guidance on post-treatment family building, consideration of the patient's understanding of the consequences of cancer and cancer therapy on offspring becomes even more germane.[3]

There is no medical evidence that cancer therapies present a risk for congenital abnormalities in offspring[4] and, in the absence of a hereditary cancer syndrome, there is no increased incidence of genetic disease in offspring of cancer survivors.[5] Studies have described adverse pregnancy outcomes in childhood cancer survivors noting increased rates of prematurity, low birth weight, and miscarriage, specifically where treatment involved abdominal radiation.[6] Few studies have evaluated YAFCSs' concerns about cancer-related health risks to offspring and genetic risk heritability. Estimates suggest that 14%–35% of young patients believe their cancer treatment could cause health problems for future children, with another 37% unsure of health risks.[7,8] Some evidence points to a lack of knowledge or confusion about treatment effects (e.g., fears of ''defective genes'' due to radiation exposure) as a source of fears related to genetic inheritance.[9] Survivors of adolescent cancer have expressed an imagined feeling of responsibility regarding the potential health problems of future children with some reporting a decreased desire for children due to this concern.[10] Notably, worries may persist despite receiving information from clinicians that concern about genetic risk heritability from cancer treatment was unfounded.[10]

Although there is an emerging body of literature suggesting that infertility is among the more distressing survivorship topics for YAFCSs,[11] it is unclear how concerns about future offspring's health contribute to this distress. The field of genetic counseling has shown that patients' subjective estimate of cancer risk tends to be higher than actual risk, but is reduced with the receipt of targeted, individualized counseling.[12] A first step in developing fertility counseling resources for YAFCSs is to better understand the nature of their concerns and identify those who may be at higher risk for misinformation. This study describes YAFCSs' concerns about the health of future children and perceptions of genetic risk after exposure to gonadotoxic cancer therapy. Specifically, we sought to evaluate whether concerns varied based on demographic or clinical factors and across disease subgroups based on disease heritability.

Methods

Design

Fertility-related perceptions of YAFCSs who had completed therapy were assessed using a cross-sectional

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York.
[2]Survivorship Center, Memorial Sloan Kettering Cancer Center, New York, New York.
[3]Department of Medicine, Hofstra Northwell School of Medicine, Manhasset, New York.
[4]Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, New York.

internet-based survey.[13] This secondary analysis focused on concerns related to the health of future children specifically. Surveys were administered between February and March 2015. This study was approved by the Memorial Sloan Kettering Cancer Center (MSK) Institutional Review Board/Privacy Board.

The survey was designed by an interdisciplinary team and incorporated feedback from YAFCSs. The survey was anonymous, and protected health information was not collected. Standard questions assessed sociodemographic, medical, and fertility-related information as reported by the patient. The survey was administered online using a commercially available website with secure sockets layer encryption. Participants were recruited through MSK and 17 young adult cancer survivor advocacy groups using social media and email listservs. These procedures are consistent with recommended use of social media in young adult oncology research[14–16] and similar to previously published studies with this population.[17,18] Respondents were required to answer screening items to confirm eligibility.

Participants

Eligibility criteria included female cancer survivors 18–35 years old, who had completed treatment and were disease free. This secondary analysis excluded respondents who reported they did not desire future children or who had been told they were infertile or unable to carry a pregnancy.

Measures

The 3-item Child's Health Subscale (CHS) is a subset of the 18-item, validated Reproductive Concerns after Cancer Scale (RCACS). The other five subscales in the RCACS include (three items each) Fertility Potential, Partner Disclosure, Personal Health, Acceptance (reverse coded), and Becoming Pregnant.[1] The CHS consists of three questions: (1) I am worried about passing on a genetic risk for cancer to my children, (2) I am worried how my family history might affect my children's health, and (3) I am afraid my children would have a high chance of getting cancer. Each question was evaluated individually. Participants responded on a five-point Likert scale from ''Strongly disagree'' to ''Strongly agree.'' The subscale score ranges from 3 to 15. Higher scores indicate greater reproductive concerns (Cronbach's alpha = 0.83).

Data analysis

Secondary analyses were conducted on participants with complete data on the CHS. Descriptive statistics characterized subscale responses and sociodemographic and clinical data. Independent *t*-tests compared subscale responses by sociodemographic/clinical groups. Group comparisons included race, education level, and cancer diagnoses. Diagnoses were differentiated between those with and those without a strong family history component (breast, colorectal, and ovarian vs. all other cancer types), as identified in National Comprehensive Cancer Network guidelines for adolescent and young adult oncology.[2] Pearson's correlation assessed the relationship between age and subscale responses.

Results

Seven hundred fourteen YAFCSs accessed the survey, with 359 meeting initial eligibility screening criteria. Of eligible respondents, 346 completed the survey in its entirety; respondents who expressed a desire for future children had not been previously told they were infertile, and those who completed the entire CHS were included in this analysis, with a final sample of 187 (Table 1). Only 29 participants (8.4%) who met initial eligibility criteria reported that they ''definitely did not'' want (more) children in the future and were excluded from analyses. There were no differences in demographic or clinical characteristics between the subgroup analyzed in this report and the other respondents in the sample ($p > 0.05$). Within this subgroup, average age at the start of treatment was 23.7 years (standard deviation [SD] = 7.2, range 0–34), and mean current age was 29.5 years (SD = 4.1, range 18–35). Respondents were on average 4.4 years (SD = 4.9, range = 0–26) from treatment completion. The most common cancer diagnoses were lymphoma, breast, leukemia, ovarian,

Table 1. Sociodemographic and Clinical Data of the Study Sample of Young Adult Female Cancer Survivors ($N = 187$) Who Completed the Child's Health Subscale

	M (SD)	*Range*
Age at diagnosis (years)	23.7 (7.2)	0–34
Age at survey completion (years)	29.5 (4.1)	18–35
Duration of survivorship (years)	4.4 (4.9)	0–26
	n	%
Total	183	100
<15 years of age at diagnosis	20	11
Race		
White	162	89
Other	18	10
No response	3	2
Hispanic ethnicity	14	8
Education		
<College degree	40	22
≥College degree	143	78
Enrolled student (full or part time)	43	24
Employed (full or part time)	149	80
Annual household income		
Had at least one child	50	27
Diagnosis[a]		
Lymphoma	54	29
Breast	41	22
Other	29	16
Leukemia	15	8
Ovarian	14	7
Colorectal	13	7
Sarcoma	11	6
Brain	5	3
Cervical	2	1
Uterine	2	1
Lung	1	1
Genetic risk diagnosis	68	36
Treatment[a]		
Surgery	4	2
Chemotherapy	155	83
Radiation	14	8
Bone marrow transplant	6	3

[a]Not mutually exclusive.
SD, standard deviation.

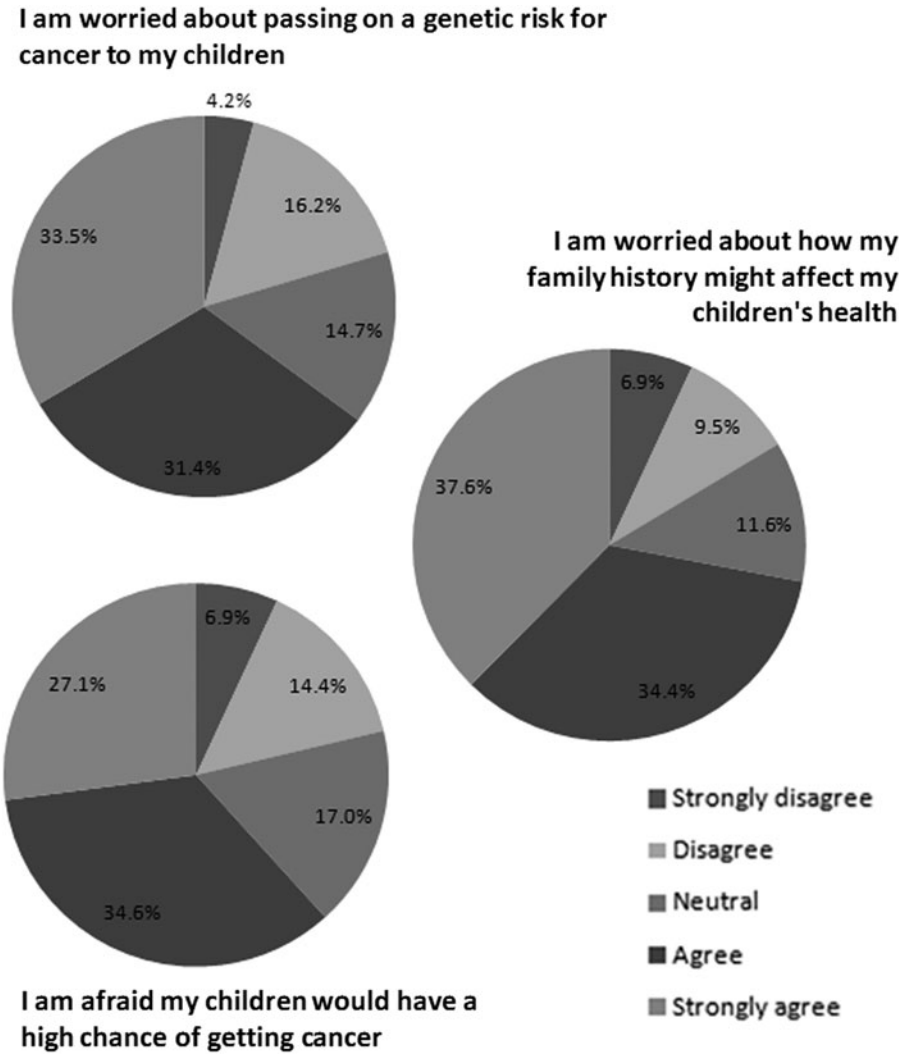

FIG. 1. Young adult female cancer survivors' responses to the Child's Health Subscale, depicting concern about heritable health risk.

and colorectal. Most participants were married or living with a partner (62%), earned a college degree or higher (78%), and were employed full or part time (80%).

The mean total CHS score was 11.3 (SD = 3.3, range 3–15). As noted in Figure 1, at the item level, 65% of YAFCSs were worried about passing on a genetic risk for cancer to offspring, with 34% of respondents indicating the highest level of agreement by responding *strongly agree*. Sixty-two percent were afraid that their children would have a high chance of getting cancer, with 27% *strongly agreeing*. Seventy-two percent were worried about how their family history would affect their children's health, with 38% *strongly agreeing*.

The CHS scores were not correlated with age at diagnosis or age at time of survey nor did they vary by marital status, race, prior children, or education level (Table 2). Diagnoses were divided into two categories based on how likely the disease is to be associated with a transmissible genetic mutation (actual data about each respondent's genetic status were not available). When comparing CHS scores between patients with diagnoses most likely to be associated with a transmissible genetic mutation (breast, ovarian, and colorectal cancer) (mean = 11.2, SD = 3.4) and all other diagnoses (mean = 11.3, SD = 3.2), there was no variation ($t = 0.28$, $df = 185$, $p = 0.78$). In both groups of patients, 65% of YAFCSs expressed concern related to genetic risk for cancer in offspring, suggesting the possibility of an inappropriate or unnecessary concern among those respondents who did not have a heritable diagnosis.

Discussion

We previously reported that YAFCSs have substantial unmet information and support needs related to fertility and family building post-treatment.[13] This analysis was conducted to better understand a particular aspect of reproductive concern

TABLE 2. RESULTS OF BIVARIATE STATISTICS FOR CHILD'S HEALTH SUBSCALE SCORES

Variable	*Mean difference*	*Standard error*	*t/r*	*df*	p
Race	0.41	0.80	0.51	178	0.61
Education	0.13	0.59	0.23	181	0.82
Marital status	0.08	0.51	0.16	185	0.87
Prior children	0.76	0.65	1.2	185	0.25
Genetic risk diagnosis	0.14	0.50	0.28	185	0.78
Age at diagnosis			<0.01	—	0.99
Age at survey			0.01	—	0.87

pertaining to concern about the health of future children. Our findings are consistent with the limited available literature,[10] as the majority of respondents noted concerns about future children's health: 65% worried about passing on a genetic cancer risk, 62% were afraid children would have a high chance of getting cancer, and 72% were worried how their family history might affect their children's health.

There were no differences in concern in our sample based on the association of their cancer diagnoses with a transmissible genetic mutation. These findings suggest there may be a subgroup of YAFCSs with inappropriate genetic risk concern (i.e., without substantiated medical evidence to suggest genetic heritability) or a subgroup who are uninformed about their genetic risk profile. Inappropriate genetic concern may be related to misinformation or mistaken beliefs regarding inheritance patterns of their disease. Owing to the anonymous and self-report nature of the study, it is unknown whether the respondents actually had a transmissible genetic mutation, what genetic risk information they received, if any, in the course of their cancer treatment, or whether they sought information from other sources such as other healthcare providers, friends, family, or websites. Understandably, a survivor may be fully aware of the heritability status of her cancer and still be concerned or not.

Nevertheless, there are a number of reasons patients may have misconceptions about the health of future children. They may mistakenly believe that prior cancer treatment will cause permanent genetic mutations in surviving oocytes, negatively impacting the health of children conceived after treatment.[19] The trend toward personalized medicine in cancer treatment, such as genomic profiling for targeted therapy, also opens opportunities for misunderstanding among patients. For example, patients have reported beliefs that genetic mutations found in tumor cells are transmissible to future offspring.[20] Increasing public awareness of genetic health risks, the growing popularity of commercially available germline testing, and the high incidence (17.7%) of variants of unknown significance further complicate discussions of hereditary risk.[21,22] Research shows ongoing difficulty in presenting these complex genomic concepts to patients.[23]

There were several limitations to this study. Owing to concerns about participant burden, more detailed information about the reasons for YAFCSs' concerns about children's health and genetic risk was not available. The survey was anonymous, precluding validation of participant responses or further comparison between eligible and ineligible patients. Cancer diagnosis was based on self-report of disease type, and individual heritable genetic risk profiles were unknown. It is unknown whether participants answered the survey item about family health history in reference to cancer genetic risk exclusively or risks for other medical conditions. Participants were recruited through social media and were a racially/ethnically homogenous and relatively well-educated group, which compromises the generalizability of the results. Assessment of genetic risk concern was limited to survivors' consideration of future children. It is also true that survivors may be concerned about children conceived before their diagnosis as well as risk related to pregnancy after treatment. It may be important to tailor patient resources and genetic counseling services to patient subgroups with varying informational and support needs. Future research is needed to better understand YAFCSs' knowledge and concerns about genetic heritability and childbearing risks and to develop and assess counseling strategies around this specific fertility and family-building topic in post-treatment survivorship.

When discussing survivorship care with YAFCSs, providers should initiate discussions about family building plans. It may be important that providers elicit YAFCSs' concerns about the health of future children and clarify misconceptions. If the patient has a heritable syndrome, providers should make referrals for genetic counseling. For YAFCSs with an identified heritable genetic mutation, such as BRCA1 or BRCA2, counseling may include a discussion of preimplantation genetic diagnosis, which may alleviate some concern about passing on genetic risks.[24]

Conclusion

Many YAFCSs have concerns about the health of future children, particularly related to family history and passing on a genetic risk for cancer. Future research should build on this preliminary study with more comprehensive measures of genetic concerns and in conjunction with valid medical information about genetic and other health risks to future children. Educating patients about this aspect of reproductive health, and tailoring information based on actual risk, or lack of risk, may reduce distress about childbearing and facilitate family-building decisions.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Nirupa Jaya Raghunathan, MD
Department of Medicine
Memorial Sloan Kettering Cancer Center
485 Lexington Avenue, 2nd Floor
New York, NY 10017

Email: raghunan@mskcc.org