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Author manuscript

Support Care Cancer. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

Support Care Cancer. 2016 July ; 24(7): 3191–3199. doi:10.1007/s00520-016-3138-x.

Young female cancer survivors' use of fertility care after completing cancer treatment

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Abstract

Purpose—To investigate factors associated with female young adult cancer survivors' (YCS) use of fertility care (FC), including consultation or fertility treatment, after completing their cancer treatment.

Methods—In this cross-sectional study, females between that ages of 18 and 35 years who had been diagnosed with childhood, adolescent, or young adult cancers completed a 20-min web-based survey that included demographics, reproductive history, use of FC, fertility-related informational needs, and reproductive concerns.

Results—A total of 204 participants completed the survey. Participants' mean age was 28.3±4.5 years. Thirty (15%) participants reported using FC after cancer treatment. The majority of participants recalled not receiving enough information about FP options at the time of cancer diagnosis (73%). In multivariable analysis, those with higher concerns about having children because of perceived risk to their personal health ($P=0.003$) were less likely to report use of FC after cancer treatment. Those who had used FC before cancer treatment ($P=0.003$) and who felt less fertile than age-matched women ($P=0.02$) were more likely to use FC after their cancer treatment.

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Competing interest(s) There is no competing interest.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

Conclusions—While most YCS in this cohort believed that they did not receive enough information about fertility and most wanted to have children, the vast majority did not seek FC. The findings of this study offer further evidence of the need for improved education and emotional support regarding reproductive options after cancer treatment is completed. Targeted discussions with YCS about appropriate post-treatment FC options may improve providers' capacity to help YCS meet their parenthood goals.

Keywords

Fertility care; Cancer survivor; Cancer treatment; Female

Introduction

Infertility is one of the most common long-term problems reported by female young cancer survivors (YCS) [1]. Cancer treatments such as radiation and chemotherapy have significant potential to cause damage to ovarian germ cells, which would lead to a range of future scenarios, including sterility, early menopause, diminished fertility, or no problems at all [2–4]. YCS are less likely to report pregnancy than their siblings or population control subjects [5–7]. There are also studies reporting a higher rate of premature ovarian failure in YCS compared to their female siblings [4, 8]. Infertility can have a significant impact on a woman's life after cancer, affecting her personal relationships, future family planning, and concerns about pregnancy and birth [9, 10]. Considering the high survival rate in cancer patients [11], reproductive concerns resulting from cancer treatment are an important quality of life (QOL) issue among YCS [12].

Due to the heightened awareness of QOL after cancer including reproductive health, the topic of fertility care (FC) has evolved in clinical importance and, in turn, there is a higher demand from the patients themselves [13]. While most current FC efforts focus on preserving fertility prior to cancer treatment, FC after cancer treatment is also important in terms of monitoring reproductive health and exploring FC and other options to assist patients who are ready to start a family. With the low uptake rate of fertility preservation treatment prior to cancer treatment [14], it may be even more important to offer FC, including fertility treatment where appropriate, after cancer treatment to patients who missed the opportunity prior to their cancer treatment. While it is recommended for survivors of childhood, adolescent, and young adult cancer to be referred to a fertility specialist to discuss and monitor their reproductive health after cancer treatment [15], there is a paucity of data about the frequency of their pursuing FC after cancer treatment.

We aim to describe YCS' use of FC after completing cancer treatment and the factors related to use of post-treatment FC. To evaluate our question, we analyzed web-based survey data from a diverse group of female YCS.

Patients and Methods

Participants and procedures

Between March and September 2012, we enrolled female young adult-aged cancer survivors to complete a 20-min web-based survey. The primary goal of the cross-sectional study was to determine the reproductive health outcomes and concerns of YCS. The study recruited female YCSs between the ages of 18 and 35 years who had childhood, adolescent, or young adult cancers. This age range represents women in their reproductive years when fertility and pregnancy rates are highest in the general U.S. population [16]. All participants were at least one year post-diagnosis, not currently pregnant, and English-speaking. Eligibility criteria did not include current cancer treatment status. Most participants were recruited via online social media outlets and local community outreach efforts [17]. Potential participants completed a web-based screening form and, if eligible, were provided electronic informed consent and then linked to the web-based survey. Eighty six percent of those eligible completed the survey. The University of California, San Diego Institutional Review Board approved the study.

Data collection and measurement

The web-based survey collected self-reported information about demographics, cancer characteristics including diagnoses and type of treatment received, and reproductive history including pregnancy attempts, births, miscarriages, and infertility. We assessed reproductive history and pregnancy plans using standard questions from the National Survey for Family Growth (e.g., pregnancy and birth outcomes; desire for children) [18]. We used the Time to Pregnancy measure to evaluate time between initiating an attempt to conceive and conception, with more than 12 months indicating infertility [19], and the Penn Ovarian Aging Study Menstrual Questionnaire to evaluate menstrual pattern data over the past year [20].

Patient-provider communication about fertility at the time of cancer diagnosis was assessed by a series of questions, such as, “Before your cancer treatment began, did a doctor, nurse, or other medical professional talk with you and/or your family about the possible impact of cancer treatment on your future fertility (ability to become pregnant)?” We further characterized participants’ fertility-related information needs at the time of cancer diagnosis using the following three items, “Thinking back to the time of your cancer diagnosis and information that you or your family may have wanted or needed about fertility or fertility preservation options, please say whether you strongly disagree, disagree, neither agree nor disagree, agree, or strongly agree with each statement. I and/or my family 1) Needed information that we did not know how to get about fertility after cancer treatment and FP options; 2) Received enough information from a medical professional about how my future fertility could be impacted by my cancer treatment; and 3) Were too overwhelmed at the time of my cancer diagnosis to consider how my fertility could be impacted by my cancer treatment.” These survey items were pilot tested, and refined during a series of focus groups and cognitive interviews with young female cancer survivors [21]. This process focused on ensuring that items were understood as intended.

The 18-item Reproductive Concerns After Cancer (RCAC) scale measures feelings about having biological children now or in the future [22]. It includes the following six subscales, each of which has been shown to have high internal consistency (as reflected by Cronbach's α): Fertility potential ($\alpha = 0.86$) (e.g., "I am afraid I won't be able to have any (more) children"); Partner disclosure of fertility status ($\alpha = 0.88$) (e.g., "I worry about telling my (potential) spouse/partner that I may be unable to have children"); Child's health ($\alpha = 0.88$) (e.g., "I am worried about passing on a genetic risk for cancer to my children"); Personal health ($\alpha = 0.83$) (e.g., "I am scared of not being around to take care of my children someday"); Acceptance of possibly not having children ($\alpha = 0.82$) (e.g., "I can accept it if I'm unable to have (more) children"); and Becoming pregnant ($\alpha = 0.78$) (e.g., "I worry that getting pregnant (again) would take too much time and effort"). The response scale uses a five-point Likert scale ranging from 1="Strongly disagree" to 5="Strongly agree" [22].

Participants also reported on their perceived fertility compared to other women their age, importance of having biological children, whether cost had ever prevented them from using FC, and use of FC before and after their cancer treatment.

The primary outcome was defined as the use of FC (fertility treatment and/or consultation with a fertility specialist) after completing cancer treatment. Fertility treatment was defined by exposure to fertility drugs (such as recombinant gonadotropins and oral ovulation induction drugs) and/or assisted reproductive techniques (ART, such as intrauterine insemination and in vitro fertilization).

Statistical analysis

Descriptive statistics were used to characterize the study cohort, and were calculated as frequency and percentage for categorical data and mean and standard deviation (SD) for continuous data. To avoid assumptions of linearity, continuous variables were dichotomized for subsequent statistical analysis based of the clinical implication (e.g.: having fewer than 10 periods in 12 months is defined as abnormal menstrual period pattern) and statistical representativeness (e.g.: median value). Summary RCAC scores were calculated for each subscale and for the scale as a whole, with higher scores indicating more concern [23]. Associations of use of FC with demographics, reproductive and cancer history and perception about future parenthood and own fertility were evaluated by first categorizing continuous variables and then using chi-square tests or Fisher's Exact test. With the exception of cancer type, categorizations were all dichotomous in order to avoid issues with small cell sizes. Age, which was considered to be clinically related to the use of FC, and variables that were statistically significant ($p < 0.05$) determinants of the use of FC in the bivariate analysis were considered for inclusion in the multivariable model. The final model was specified using backward selection from this list as initial covariates. Those with a p-value of less than 0.10 were retained in the final model. Statistical analyses were conducted using SAS version 9.3 (Cary, NC).

Results

A total of 204 participants completed the survey. Their mean ages at cancer diagnosis and study participation were 22.9 ± 7.6 years and 28.3 ± 4.5 years, respectively. At participation,

6% were age 20 or younger, 24% were 21–25, 33% were 26–30, and 38% were 31–35 years old. Mean time since cancer diagnosis was 5.7 ± 5.4 years. The majority of subjects (72%) had an education level of college graduation or more (Table 1). Eighty percent of the participants were white and 49% were currently in a relationship. Most subjects were nulliparous at the time of cancer diagnosis (87%) and study participation (83%). Fifty-nine women (29%) had ever tried to conceive, and, of those, 15 (25%) reported a history of infertility (unable to get pregnant after more than one year of trying) before cancer diagnosis.

Hematologic cancer (37%) was the most common cancer diagnosis followed by breast (17%) and gynecologic (7%) cancers. Three fourths of participants (75%) received chemotherapy for cancer treatment and 38% of those reported received alkylating chemotherapeutic agents.

Forty-one participants (20%) had had a consultation with a fertility specialist between their cancer diagnosis and the commencement of cancer treatment, and among those, 19 (46%) had pursued ART. Eight patients (20%) had used gonadotropin-releasing hormone agonist to suppress their ovaries. About a quarter of participants ($n=55$, 27%) reported receiving enough information from a medical professional about FP options at the time of their cancer diagnosis. Most ($n=131$, 64%) reported that they were too overwhelmed at the time of their cancer diagnosis to consider FP options (strongly agree or agree that they were too overwhelmed) (Table 2).

Use of fertility care after cancer treatment

Of 204 participants, 30 (15%) sought FC after cancer treatment. A consultation with a fertility specialist was the most common type of FC (28 out of 30 participants, 93%). Eight participants (4%) used fertility drugs or pursued ART.

In unadjusted analyses, history of infertility before cancer diagnosis was significantly associated with the greater use of FC after cancer treatment ($P=0.03$). Women who had regular menstrual cycles (10 or more periods in the past 12 months) were less likely to use FC after cancer treatment ($P=0.005$). Demographics such as age, race, education, parity, partner status, duration of survivorship and the type of cancer and cancer treatments were not associated with the use of FC after cancer treatment (Table 1).

Participants who saw a fertility specialist before their cancer treatment were also more likely to pursue FC after their cancer treatment ($P < 0.0001$). Those who felt too overwhelmed at the time of diagnosis to consider FP options were less likely to pursue FC after cancer treatment ($P=0.01$). However, receiving enough information about FP options at the time of cancer diagnosis was not associated with the use of FC after cancer treatment ($P=0.97$) (Table 2).

Participants who felt that they were less fertile than other women of their age were more likely to have used FC after cancer treatment compared to participants who felt that they were as fertile as or more fertile than women their age ($P=0.005$). While about three-quarters of participants reported that having biological offspring was important or very important in their lives, this characteristic was not related to use of FC after cancer treatment ($P=0.40$).

FC use after cancer treatment was not associated with overall degree of reproductive concerns as reflected by the RCAC score ($P=0.59$). However, women who did not pursue FC after cancer treatment had greater levels of reproductive concerns related to their personal health compared to women who did access FC ($P=0.003$) (Table 3).

In multivariable analysis, participants who had higher reproductive concerns related to their personal health (OR 0.81 [95% CI: 0.71, 0.93], $P=0.003$) were less likely to have pursued FC after cancer treatment. On the contrary, participants who had pursued fertility consultation prior to cancer treatment were more likely to use FC after cancer treatment (OR 3.91 [95% CI: 1.61, 9.55], $P=0.003$). Those who felt less fertile than age-matched women also had higher odds of seeking FC after cancer treatment as compared to women who felt as fertile or more fertile than women their age (OR 4.60 [95% CI: 1.26, 16.79], $p=0.02$). Estimates from multivariable models were not substantially different from unadjusted models (Table 4).

Discussion

Previous reports show that a threat to future fertility is a significant concern for female YCS [24–26], and that patients are receiving inadequate or conflicting information regarding FP [27], are uncertain about their fertility status, and feel regret about not having options [28, 29]. Despite the heightened awareness of the importance of fertility and discussion of FP options with YCS, only a small proportion of patients receive FC either before or after their cancer treatment [14, 30–32]. There are several studies reporting characteristics of the participants who seek for FC prior to initiation of treatment [14, 27], this is the first to investigate the characteristics of the participants who seek for FC after the completion of treatment. In our study of YCS, where the average age was 28.3 years and average duration of survivorship was 5.7 years, only 15% of participants had accessed FC after cancer treatment and only 4% had used fertility drugs or pursued ART. This represents an important target audience for improved survivorship care because young women who have had gonadotoxic cancer treatment can face a shorter than expected window of fertility [28, 33, 34]. It is important for those desiring biological children to seek medical advice as soon as possible after completing their treatment to preserve their parenthood options.

The acquisition of information is related to patients' high-quality decision making [35]. Correspondingly, this study found that exposure to fertility information before cancer treatment is associated with higher uptake of FC after completing treatment. Patients who saw a fertility specialist before their cancer treatment also tended to have follow-up monitoring with a fertility specialist after cancer treatment. Only 30 women in this study initiated FC after their cancer treatment, and 13 (43%) of those had also reported FC prior to their cancer treatment. This suggests a need for improved knowledge of and access to post-treatment FC options for young survivors who want to have children.

An individual's perceived need for medical care is one of the major promoting factors of healthcare-seeking behavior [36]. In the multivariable model, those who reported feeling less fertile than age-matched women had significantly higher odds of using FC after their cancer treatment. This is in line with the trend for lower odds of post-treatment FC that we

observed among women having normal periods in the past year, although this variable did not emerge as a significant predictor in the multivariable model. Those who feel more fertile or are reassured of their fertility by regular menstrual periods may be at a disadvantage when making decisions about FC after cancer treatment because post-treatment menstrual pattern is not a reliable marker of fertility [5]. Unexpectedly, we found no difference in use of FC after cancer between women who said that biological offspring were important to them compared to those who did not. This could be explained by lack of knowledge about the medical options available and advantage of FC after cancer treatment. Improved counseling and education focused on the options available to monitor and preserve fertility after cancer treatment may be of benefit to those YCS who want to have biological children.

A decision to pursue parenthood is complex, and there are even more factors to consider for cancer survivors and women with chronic health conditions [22]. In our study, YCS who were more concerned about their personal health (i.e., the potential impact of a recurrence or survival on their children) had lower odds of accessing FC after their cancer treatment. Qualified emotional support in survivorship, such as by a clinical psychologist or social worker, can provide an important and needed opportunity for YCS to discuss such concerns and may also improve communication between YCS and their other healthcare providers [37]. This also underscores the importance of a multidisciplinary approach to managing the overall health of cancer survivors. A better understanding of how women cope with their personal health concerns in relation to their decisions about parenthood could assist in the development of improved processes and communication tools to support the overall health of YCS.

Despite the growing focus on the importance of fertility for YCS, this is the first study to evaluate factors associated with female YCS' use of FC after completing their cancer treatment. While it remains a priority to discuss FP options at the time of cancer diagnosis, many feel unprepared to fully consider their options at that time. Improved access to FC after cancer treatment provides an important opportunity for education and support, and could lead to more available options for biological parenthood, such as through ovarian reserve monitoring and earlier or more aggressive fertility treatments. This study also provide insight on key factors that are related to the patients' uptake of FC after their cancer treatment, which could help in the development of an improved patient care system to provide appropriate post-treatment FC and FP options to those who are considering future parenthood.

Our study has several limitations. First, the cross-sectional design limits our ability to make causal inferences. For example, it is possible that women who reported higher odds of seeking FC after their cancer treatment felt less fertile because of information that had been provided to them during a fertility consultation, rather than seeking care because they felt less fertile. We did not directly assess reasons for accessing FC before and after cancer treatment or YCS' perceptions about infertility risk based on treatment regimen. It is interesting that only a fraction of participants (25%) reported that they had FC before their cancer treatment, but our study cannot determine if this is due to recall bias, barriers such as limited access, personal preferences, or other reasons. Longitudinal studies are needed to provide insight regarding when and why YCS access, or fail to access, fertility-related

services. The sample size and the heterogeneity of our sample also limit our ability to adjust for all potential confounders, including cancer type and treatment. It is possible that some women did not recall use of fertility-related services before or after cancer; we did not collect medical record data, so we do not have formal documentation of these visits. Because many participants were recruited from social media and chose to participate in a fertility-focused research study, they may be more interested in this topic than the general YCS population, which may limit generalizability.

In conclusion, while most YCS in this cohort reported wanting to have children and believed that their fertility may have been compromised, only a small proportion reported using FC after completing their cancer treatment. Post-treatment FC represents an important opportunity for intervention and education earlier in survivorship that could keep the option of biological parenthood open for young survivors who are considering future parenthood. Comprehensive survivorship care to monitor reproductive health, assess parenthood intentions, address reproductive concerns, and provide emotional support could facilitate decision-making and appropriate referral for consultation about fertility. Studies that further explore unmet needs and barriers related to FC after cancer could assist in the development of targeted approaches and communication tools to support the overall health of YCS who are considering biological children.

Acknowledgments

This study was initiated and conducted with the support of the American Cancer Society grants #120500-PFT-11-008-01-CPPB and #ACS IRG 70-002. This study was funded (in part) by the National Cancer Institute, Comprehensive Partnerships to Reduce Cancer Health Disparities Program, grants #U54CA132384 and #U54CA132379, National Institutes of Health (National Institute of Child Health and Development) grant #HD058799 and #5TL1CA133837-05, and American Cancer Society grant #MRSG-08-110-01-CCE.

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Table 1

Demographic and medical determinants of use of fertility care services after cancer treatments (N=204).

	Use of fertility care <i>after</i> cancer treatment		
	Yes (n=30) n (%)	No (n=174) n (%)	<i>P</i> -value
Demographics			
Age (yrs)	29.4±5.1	28.1±4.4	0.16
30	15 (12)	112 (88)	0.13
>30	15 (19)	62 (81)	
Education			0.38
Did not complete college	6 (11)	51 (89)	
Completed college	24 (16)	123 (84)	
Race			0.33
Caucasian	22 (14)	141 (87)	
Non-Caucasian	8 (20)	33 (80)	
Relationship status			0.84
Married or committed relationship	19 (16)	103 (84)	
Not in a relationship	11 (14)	71 (87)	
Employed			0.79
Yes	25 (15)	147 (85)	
No	5 (16)	27 (84)	
Current healthcare insurance			0.99
Yes	29 (15)	165 (85)	
No	1 (10)	9 (90)	
Reproductive History			
Nulliparous at study participation			0.61
Yes	24 (14)	145 (86)	
No	6 (17)	29 (83)	
Nulliparous at cancer diagnosis			0.38
Yes	28 (16)	149 (84)	
No	2 (7)	25 (93)	
Number of periods in the past 12 months			0.005
10	11 (37)	19 (63)	
9 or less	111 (64)	63 (36)	
Infertility at time of cancer diagnosis ^a			0.03
Yes	7 (47)	8 (53)	
No	7 (16)	37 (84)	
Cancer characteristics and treatment			
Cancer type			0.64

	Use of fertility care <i>after</i> cancer treatment		
	Yes (n=30) n (%)	No (n=174) n (%)	P-value
Hematologic	8 (11)	66 (89)	
Breast	6 (17)	29 (83)	
Gynecologic	3 (10)	27 (90)	
Thyroid	5 (24)	16 (76)	
Soft tissue	1 (8)	11 (92)	
Brain	1 (8)	11 (92)	
Other ^b	6 (30)	14 (70)	
Life stage at cancer diagnosis			0.55
Childhood (< 14 yrs)	5 (19)	21 (81)	
Adolescence (15 – 20 yrs)	3 (13)	21 (88)	
Young adulthood (20 – 35 yrs)	22 (14)	132 (86)	
Cancer stage or risk group			0.99
Advanced stage ^c	10 (15)	57 (85)	
Early stage ^d	20 (15)	117 (85)	
Higher risk cancer treatment			
Alkylating chemotherapy	13 (18)	59 (82)	0.41
Bone marrow or stem cell transplant	4 (25)	12 (75)	0.26
Duration of survivorship (yrs)			0.07
1 – 4	15 (11)	117 (89)	
5 or more	15 (21)	57 (79)	
Cancer recurrence			0.29
Yes	7 (21)	27 (79)	
No	23 (14)	147 (86)	

^aInclude 59 women who had ever tried to get pregnant

^bIncludes bone (6), genitourinary (2), lung (2), gastrointestinal (9) and thorax-pharynx (1) cancers

^cStage 3 or more

^dStage 2 or less

Table 2

Association between accessibility to fertility care services and financial barriers at cancer diagnosis, and the use of fertility care services after cancer treatments (N=204).

	Use of fertility care <i>after</i> cancer treatment		
	Yes (n=30) n (%)	No (n=174) n (%)	P-value
Had fertility care before cancer treatment			<0.0001
Yes	13 (32)	28 (68)	
No	17 (10)	146 (90)	
Needed information that we did not know how to get about fertility after cancer treatment and FP options			0.09
Yes	17 (20)	70 (80)	
No	13 (11)	104 (89)	
Received enough information from a medical professional about fertility after cancer treatment and FP options			0.67
Yes	11 (13)	71 (87)	
No	19 (16)	103 (84)	
Were too overwhelmed at the time of diagnosis to consider my fertility after cancer treatment and FP options			0.01
Yes	13 (10)	118 (90)	
No	17 (23)	56 (77)	
After cancer diagnosis, the cost has ever prevented you from using any FC^a			0.89
Yes	9 (20)	35 (80)	
No	18 (21)	66 (79)	

^aSeventy-six women were not applicable for this question

Table 3

Association between perception about own fertility and future offspring and Reproductive Concerns After Cancer (RCAC) scale, and the use of fertility care services after cancer treatments (N=204).

	Use of fertility care <i>after</i> cancer treatment		
	Yes (n=30) n (%)	No (n=174) n (%)	P-value ^d
Feeling about own fertility			0.005
Fertile	3 (5)	59 (95)	
Less fertile	27 (20)	110 (80)	
Important to have biologic offspring^a			0.40
Yes	24 (17)	121 (83)	
No	6 (11)	48 (89)	
RCAC summary score^b (Mean±SD)	57.5±11.7	58.7±10.9	0.59
RCAC subscale scores^c (Mean±SD)			
Fertility potential	11.5±3.6	10.6±3.2	0.07
Partner disclosure	8.9±4.1	9.6±3.6	0.33
Child's health	10.0±3.6	11.2±3.4	0.12
Personal health	8.3±2.5	10.3±3.4	0.003
Acceptance	9.1±3.2	7.9±2.8	0.06
Becoming pregnant	9.7±2.3	9.2±2.9	0.33

^aFive women did not complete this question

^bOverall RCAC summary score, range 18–86

^cRCAC Subscale summary scores, range 3–15

^dFisher's exact test

Table 4

Multivariable analysis for determinants of use of fertility care services after cancer treatment in female YCS (N=204)

Variables	Unadjusted odds ratio (95% CI)	P-value	Multivariable adjusted odds ratio * (95% CI)	P-value
Current age (years)	1.07 (0.97, 1.20)	0.16	1.06 (0.97, 1.17)	0.20
Had fertility care before cancer treatment	3.99 (1.74, 9.12)	0.001	3.91 (1.61, 9.55)	0.003
Feel less fertile than age-matched women	4.74 (1.38, 16.26)	0.01	4.60 (1.26, 16.79)	0.02
Higher reproductive concerns about personal health ^a	0.84 (0.74, 0.95)	0.005	0.81 (0.71, 0.93)	0.003

* Multivariable adjusted model includes all variables in the table.

^aRCAC, Personal health subscale score (range 3–15)