Young Adult Female Cancer Survivors' Decision Regret About Fertility Preservation

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This study evaluated fertility-related experiences of young adult female cancer survivors (18–39 years). Data were from a retrospective, cross-sectional survey. Women were more likely to undergo pre-treatment fertility preservation (FP) if they received fertility counseling (by a fertility nurse specialist, reproductive endocrinologist, or gynecologist). Compared with women who underwent FP, those who did not had greater decision regret (DR) after treatment ($p < 0.001$). Multiple reasons for not pursuing FP were reported; lack of time and distress related to more DR and not wanting children in the future related to less DR ($p < 0.05$). Decision regret may lead to psychosocial morbidity in survivorship.

Keywords: infertility, regret, fertility preservation, fertility specialist, counseling

MANY YOUNG ADULT FEMALE CANCER (YAFC) survivors (18–39 years old) want to have children in the future¹ and are distressed about the possibility of infertility from their treatment.² With improvements in treatment and long-term survival rates, there is increased interest in YAFC survivors' fertility outcomes, as young women report potential infertility as one of the most distressing aspects of survivorship.³

The gonadotoxic effects of cancer treatments are well established.⁴ Yet, many patients report unmet information needs about fertility preservation (FP) options.^{5,6} Clinical guidelines in the United States stipulate that clinicians discuss fertility risks and FP options with all reproductive-aged patients prior to treatment.⁷ Although clinicians increasingly address fertility, many self-report they lack the necessary skills to discuss the topic with their patients, and clinician discomfort relates to a decreased likelihood of fertility discussions.^{8–10} The majority of women do not undergo pre-treatment FP, despite their plans to have children in the future.¹¹ Reasons for not undergoing FP include time constraints associated with treatment, distress surrounding the cancer diagnosis, and cost.¹² As a result, some women who successfully complete treatment may be unable to fulfill their reproductive goals in the future and experience decision-related regret.

Regret about healthcare decisions is associated with poorer physical and psychological well-being and lower quality of life (QOL).¹³ Many YAFC survivors report that making the decision to undergo pre-treatment FP is difficult and wrought with uncertainties,¹⁴ which may be associated with decision

regret and distress.^{13,15} Identifying factors that influence decision-making about FP and post-treatment regret may inform clinical care. Letourneau et al., for example, demonstrated that pre-treatment fertility counseling by a fertility specialist was associated with less regret after treatment and improved QOL.¹⁶

This study aimed to describe the decisions YAFC survivors made about FP before treatment, understand the extent of decision regret related to FP in these patients after treatment, compare characteristics of patients who preserved their fertility to those who did not, and identify factors related to increased regret among survivors.

Methods

Findings reported are secondary analyses from an anonymous, retrospective cross-sectional survey of patients' fertility-related experiences at a large, metropolitan cancer center. The study was approved as exempt from review by the Institutional Review Board.

Eligibility criteria

English-speaking male and female cancer patients, 18–45 years of age at the start of treatment, who received treatment associated with a risk of infertility (i.e., systemic chemotherapy, pelvic radiotherapy, and/or pelvic surgery with potential impact on reproductive function), and who started treatment from 2010 through 2012 were eligible to participate. Participants had to be United States residents. Based on the study aims, and to be consistent with the National Cancer Institute definition of young

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adults,¹⁷ data are reported only from female respondents who were 18–39 years of age at the start of treatment.

Measures

The survey was an investigator-designed, sex-specific self-report questionnaire, with items based on relevant literature and multidisciplinary clinical expertise. It was pilot-tested with patients and refined based on their feedback. The survey was available in paper-and-pencil format and via a web-based survey tool with SSL encryption.

Survey questions asked about FP decisions before treatment. Reasons for not undergoing FP were assessed using a checklist derived from clinical experience and the literature, and respondents were asked to select all that applied (yes/no).

The Decision Regret Scale (DRS),¹³ a 5-item validated measure of distress or remorse after a healthcare decision, was included in the survey. Participants completed this measure in reference to their decision to undergo (or not undergo) FP before treatment. Answers are on a 5-point Likert scale from “strongly agree” to “strongly disagree.” Scores range from 5 to 25, with higher scores reflecting greater regret. Internal consistency was adequate ($\alpha=0.88$).

Procedures

Potential participants were identified through a hospital database using filters based on eligibility criteria. Patients with listed email addresses were invited to participate in the online version of the survey. Patients without a known email address were sent the paper-and-pencil version with a stamped, return-addressed envelope and a letter inviting participation, with instructions to complete the survey electronically if preferred. Instructions specified that participants should complete the survey only one time.

Statistical analysis

Descriptive analyses were conducted to characterize the data. Bivariate relations were tested using Pearson's correlation and chi-square tests. Odds ratios were calculated to compare subgroups of participants on the likelihood of receiving counseling and undergoing FP. Independent samples *t*-tests evaluated differences in decision regret between women who did and did not undergo FP and between reasons for not pursuing FP and decision regret. Multiple regression evaluated the strength of associations between reasons for not pursuing FP and post-treatment decision regret, controlling for age at start of treatment and pre-treatment fertility counseling (yes/no; selected *a priori*).

Results

Table 1 shows sociodemographic and clinical data. Respondents ($N=159$) were on average 33 years old ($SD=5.0$) at the start of treatment, mostly white (76%), non-Hispanic/Latina (81%), well educated, and at least 1 year post-treatment (56%). Breast cancer (58%) and Hodgkin lymphoma (17%) were the most common diagnoses. At the start of treatment, 81% were partnered, and 45% had at least one child. Most women believed their disease was curable (88%), and either wanted children in the future (62%) or were unsure (16%).

Fertility counseling referrals

The majority of women (89%) reported that their oncologist discussed fertility with them before treatment, and 42% were offered a referral for fertility counseling to a fertility nurse specialist, reproductive endocrinologist, or gynecologist. When excluding women who reported they had not been interested in a referral ($n=54$), the rate of referral was 63%. Patients without children were 2.5 times more likely to be referred for counseling than patients with at least one child were ([CI 1.24–5.21]; $\chi^2=6.57$, $p=0.01$).

FP

Fifty women (31%) underwent FP before treatment: 45 underwent embryo or oocyte cryopreservation, and six took medicine to suppress their ovaries (respondents could pursue more than one option). Regarding the decision to undergo FP, women who received counseling were 5.4 times more likely to undergo FP than those who did not ([CI 2.47–11.78]; $\chi^2=19.23$, $p<0.001$). Women without children were 4.9 times more likely to undergo FP than those who already had at least one child at diagnosis ([CI 2.11–11.40]; $\chi^2=14.90$, $p<0.001$).

Among the 109 women who did not undergo FP before treatment, primary reasons reported included lack of time before treatment started (39%), emotional distress (31%), not wanting children in the future (28%), cost (25%), and belief that “whatever happens is meant to be” (24%; see Table 2).

Decision regret

The average decision regret score was 10.0, indicating low regret overall ($SD=4.4$; median=10; range 5–25). Decision regret was not related to age at diagnosis or current age, race or ethnicity, partner status, prior children, treatment type, or time since treatment ($p>0.10$). Women who preserved their fertility had lower levels of regret compared with those who did not (DRS 7.9 vs. 10.9; $t[144]=-4.15$, $p<0.001$; see Table 2). Item-level analysis indicated that among women who did not undergo FP, although 61% felt they made the right decision, 26% regretted their choice, and 19% would not make the same choice again (compared with 84%, 10%, and 6% of women who underwent FP, respectively).

Decision regret in YAFC survivors who did not undergo FP

Given minimal decision regret in women who underwent FP, this study sought to identify factors related to increased regret in the subgroup of women who did not preserve their fertility before treatment. Factors related to decision regret in univariate analyses (results not shown) were fit to a regression model predicting DRS scores (Table 3). Controlling for age at diagnosis and pre-treatment fertility counseling, decision regret was greater for women who endorsed lack of time ($\beta=0.25$, $p=0.01$) and emotional distress ($\beta=0.23$, $p=0.01$) as reasons for not pursuing FP, compared with women who did not endorse those reasons; not wanting children related to less regret ($\beta=-0.39$, $p<0.001$). Pre-treatment fertility counseling was associated with less regret at the trend level ($\beta=-0.15$, $p=0.10$). The overall model accounted for 29% of the variance in DRS scores.

TABLE 1. DESCRIPTIVE INFORMATION OF SOCIODEMOGRAPHIC AND CLINICAL VARIABLES (N=159)*

Sociodemographics					
			At start of treatment		
Age (years)	M=34.8, SD=5.1, range 22–43		Age (years)	M=32.8, SD=5.0, range 20–39	
	n	%		n	%
Race ^a			Married/living with partner		
White	121	76	Yes	129	81
Black/African American	6	4	No	29	18
Asian	12	8			
Other	10	7	Had children		
Prefer not to answer	3	2	Yes	71	45
Ethnicity			No	87	55
Hispanic/Latina	10	6			
Non-Hispanic/Latina	129	81	Wanted more children		
Prefer not to answer	13	8	Yes	99	62
Education			No	25	22
≤High school degree	4	3	Unsure	35	16
Some college	12	8			
Completed college or higher	137	86			
Medical information					
Cancer type			Treatment impacting fertility ^a		
Breast	92	58	Surgery	24	15
Cervical	4	3	Radiation	14	9
Colon	4	4	Chemotherapy	140	88
Hodgkin lymphoma	27	17	Bone marrow transplant	3	2
Leukemia	2	1			
Lung	3	2	Time since treatment		
Non-Hodgkin lymphoma	8	5	Still on treatment	38	24
Ovarian	4	3	<1 year	28	18
Rectal	2	1	1–2 years	65	41
Sarcoma	3	2	2+ years	23	15
Uterine	4	3			
Other or >1 primary	4	3			

*Data not available for all participants; ≤ 4% of data (*n* = 7) was missing across variables.

^aResponse categories are not mutually exclusive.

Discussion

The decision to pursue FP before cancer treatment is a complex one, influenced by many factors. Thirty-one percent of women in our sample underwent FP. Rates of women pursuing FP after a cancer diagnosis range from 2% to 41% in the literature.^{11,14,18} Women were more likely to pursue FP if they had no children at the time of diagnosis and if they received fertility counseling by a fertility nurse specialist, reproductive endocrinologist, or gynecologist.

Primary reasons for not undergoing FP in the present sample included lack of time before treatment, not wanting (more) children in the future, and cost. This is consistent with findings from Kim et al., in which desire for future children, cost, and time needed for treatment were ranked among the most influential factors in decision making about pre-treatment FP.¹² Whereas almost a third (31%) of the women in the present sample reported “emotional distress” as another major reason for not pursuing FP, only 10% of respondents in Kim et al.’s study ranked “feeling overwhelmed” as one of the top three most influential factors in their decision making. Notably, the

participants in that study were all recruited from fertility centers after a fertility consultation, and thus are not representative of all newly diagnosed patients seen in an oncology setting.

In a qualitative study of breast cancer patients, women’s decisions were influenced by three sets of factors: perceived benefits (e.g., “an insurance policy”), inhibiting concerns (e.g., financial cost, feeling overwhelmed), and influential relationships with family and physicians.¹⁹ It is important to find ways to address these inhibiting concerns, but it is also challenging, particularly in the United States where insurance coverage for FP is very limited and varies by state.^{20,21} Other factors that may influence patients’ decision making include providers’ opinions and perceptions of patients’ priorities and preferences, which influence the ways in which fertility and FP options are communicated to patients.^{22,23} Younger age and a recent start of partner relationships have also been associated with a more complicated decision-making process.^{24,25}

Women who did not undergo FP before treatment had more decision regret after treatment compared with women who preserved their fertility, but they were less likely to

TABLE 2. FERTILITY PRESERVATION AND DECISION REGRET

<i>Fertility preservation options pursued^a</i>			
	<i>n</i>	%	
Embryo or egg freezing	45	28	
Suppression of ovaries	6	4	
<i>Reasons for not pursuing fertility preservation^a</i>			
		%	
No time before treatment		39	
Too distressed		31	
Did not want (more) children		28	
Too expensive		25	
Believed “whatever happens is meant to be”		24	
Did not know about fertility preservation		9	
Too sick		5	
Did not know where to see a fertility specialist		4	
Religious beliefs		1	
<i>Decision regret scale</i>			
	Did undergo FP (<i>n</i> = 50)	Did not undergo FP (<i>n</i> = 109)	
Mean (SD) ^b	7.9 (SD)	10.9 (4.2)	<i>p</i> < 0.001
<i>DRS items</i>	%	%	
1. It was the right decision.			
Strongly agree/agree	84	61	
Neither agree or disagree	6	30	
Strongly disagree/disagree	4	5	
2. I regret the choice that was made. ^c			
Strongly agree/agree	10	26	
Neither agree or disagree	4	26	
Strongly disagree/disagree	82	56	
3. I would do the same choice again.			
Strongly agree/agree	84	55	
Neither agree or disagree	2	22	
Strongly disagree/disagree	6	19	
4. The choice did a lot of harm. ^c			
Strongly agree/agree	10	7	
Neither agree or disagree	14	19	
Strongly disagree/disagree	70	70	
5. The decision was wise.			
Strongly agree/agree	72	57	
Neither agree or disagree	10	34	
Strongly disagree/disagree	2	5	

^aRespondents may have selected more than one.^bHigher scores indicate *more* decision regret; independent samples *t*-test evaluated mean differences.^cReverse coded.

DRS, Decision Regret Scale.

experience regret if they received fertility counseling. This is consistent with other published reports indicating that regardless of whether women decide to pursue FP, fertility counseling lessens post-treatment regret.^{26,27}

Women who endorsed lack of time as a reason for not pursuing FP were also more likely to experience regret. The question in the current survey did not differentiate if this was based on medical advice, precluding FP as an option, or the patient's perception of the urgency to start treatment, so it is difficult to interpret the clinical meaning of this finding. As described above, these women may still benefit from fertility

counseling to ensure they understand the reason that FP is not an option and to lessen post-treatment regret.

Higher levels of regret were also reported by women who endorsed emotional distress as a reason for not pursuing FP. For these women, adding tailored decision support interventions to fertility counseling may help alleviate distress and improve the decision-making process, potentially decreasing post-treatment regret.^{15,28} Further research is needed to explore modifiable factors that contribute to emotional distress during decision making and to identify those patients most in need of psychosocial support. One target of

TABLE 3. MULTIPLE REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH POST-TREATMENT DECISION REGRET AMONG YAFC SURVIVORS WHO DID NOT UNDERGO FERTILITY PRESERVATION BEFORE TREATMENT

<i>Dependent variable: Decision regret,^a F(6, 94) = 7.91, p < 0.001</i>								
<i>Step</i>	<i>Variable^b</i>	<i>Adj R²</i>	<i>R²Δ</i>	<i>B</i>	<i>SE</i>	<i>β</i>	<i>t</i>	<i>p</i>
1	Covariates	−0.01	—					
	Intercept			10.78	3.02			
	Age at diagnosis			0.01	0.09	0.01	0.08	0.94
	Pre-treatment fertility counseling			−1.42	0.85	−0.15	−1.68	0.10
2	Reasons for not pursuing FP	0.29	0.34					
	No time before treatment			2.14	0.78	0.25	2.75	0.01
	Emotional distress			2.06	0.81	0.23	2.55	0.01
	Did not want (more) children			−3.60	0.86	−0.39	−4.18	<0.001
	Too expensive			−0.48	0.93	−0.05	−0.52	0.61

Women who endorsed lack of time and/or emotional distress as reasons for not pursuing pre-treatment FP reported significantly higher levels of decision regret post-treatment, compared with women who did not endorse these reasons, whereas women who endorsed “did not want more children” reported significantly less regret than women who did not endorse this item.

^aDecision regret was measured using the Decision Regret Scale (higher scores refer to greater regret).¹³

^bPre-treatment fertility counseling and reasons for not pursuing FP were dichotomized variables (yes or no) with “no” as the reference point in all cases.

YAFC, young adult female cancer; FP, fertility preservation.

intervention may be decisional conflict, which often occurs with “preference sensitive” decisions with uncertain likelihood of outcomes. YAFC patients often report high levels of decisional conflict about FP before treatment, particularly when they do not receive fertility counseling and when cost of FP services is prohibitive.¹⁹ Importantly, negative experiences during the counseling session (e.g., not enough time or not feeling supported by the counselor) have also been related to increased decisional conflict and regret.²⁴ Peate et al. demonstrated the efficacy of a decision aid intervention in reducing decisional conflict among breast cancer patients.²⁹ Chiavari et al. reported that a decisional counseling session led to reduced decisional conflict about FP, whereas medical consultation, family support, and information gathered from the internet did not explain reductions in conflict.³⁰ Future research should determine the generalizability of these findings. Interventions may also be refined to address fertility issues among patients with different support needs and at different points in post-treatment survivorship.

For patients who do not have the opportunity to preserve fertility before treatment, infertility and even the perception of impaired fertility negatively affect self-concept and esteem, dating and social relationships, and life planning.^{3,31} Addressing infertility after treatment may have beneficial effects to psychosocial well-being and QOL. Interventions may help YAFC survivors address grief around the loss of future plans related to motherhood, promote acceptance of infertility, and support alternative plans for achieving motherhood (e.g., adoption).

Limitations of this study include the cross-sectional, retrospective design, which precludes causal inferences and may reflect a response shift in respondents’ answers. Furthermore, as the survey was anonymous, it was not possible to test for potential differences between responders and non-responders, which may have biased the generalizability of the findings. Given the sociodemographic characteristics of the sample, the findings may underestimate the importance of financial cost in decision making about FP and subsequent

regret. Future work should examine the extent to which cost, health insurance coverage, and healthcare policies impact decision making about FP, particularly with respect to differences in FP coverage across countries. It is also unknown what aspects of pre-treatment experiences were most critical among those who endorsed “emotional distress” as contributing to their decision making about FP (e.g., cancer- vs. fertility-related distress). Importantly, findings reflect perceived time constraints associated with treatment, and it is unknown whether clinical data and provider recommendation would have corroborated women’s perceptions. Additionally, 24% of participants were still on active treatment (e.g., endocrine therapy), and it is unknown whether being on active treatment delays or exacerbates regret and/or fertility-related distress. These were also secondary analyses and did not include additional variables that may relate to decision regret in survivorship. Longitudinal studies in more diverse samples are needed to identify pre-treatment factors that signal YAFC survivors’ risk of experiencing long-term decision regret or distress.

Young adult survivors want fertility to be addressed in pre- and post-treatment survivorship care.³² Despite this, lack of support around fertility issues is ranked as one of their greatest unmet needs.³³ Specialized fertility counseling and psychosocial interventions to support YAFC survivors’ decisions around FP may be warranted to avoid post-treatment regret and to help women achieve their ideal reproductive and family-building goals.

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