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A Cross-Sectional Study of the Psychosexual Impact of Cancer-Related Infertility in Women: Third-Party Reproductive Assistance

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Abstract

Introduction—This study empirically assessed emotional and sexual functioning, reproductive concerns, and quality of life (QOL) of cancer-related infertile women in comparison to those without a cancer history and explored awareness of third-party reproduction options in cancer survivors.

Methods—One hundred twenty-two cancer survivors (Gynecologic and Bone Marrow/Stem Cell Transplant) with cancer-related infertility and 50 non-cancer infertile women completed a self-report survey assessing: reproductive concerns(RCS), mood(CES-D), distress(IES), sexual function(FSFI), menopause(SCL), QOL(SF-12), relationships(ADAS), and exploratory (reproductive options) items.

Results—Cancer survivors exhibited greater sexual dysfunction and lower physical QOL than non-cancer infertile women ($P<0.001$). No significant group differences were identified for mood (CES-D), mental health QOL (SF-12), reproductive concerns (RCS), and relationship satisfaction (ADAS). All groups scored in the FSFI range of sexual dysfunction, and with RCS scores above published means. Multivariate comparisons showed comparable depression and distress levels for all groups, but cancer survivors had poorer physical QOL [$F(5,146)=4.22$, $P<0.01$]. A significant effect was also found for knowledge of third-party reproductive options on depression and distress levels [$F(3,97)=4.62$, $P<0.01$]. Adjusted means demonstrated higher depression and distress scores for women with perceived unmet informational needs.

Conclusions—Overall, loss of fertility was an emotionally challenging experience for women regardless of its cause. Cancer survivors were found to have lower scores of physical QOL and sexual function than non-cancer infertile women. Unmet informational needs about reproductive options appeared to be associated with negative mood and increased distress in cancer survivors.

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Implications for Cancer Survivors—Targeted interventions to increase knowledge about reproductive options could be of great assistance to women pursuing parenthood in cancer survivorship. Additionally, intervention studies to improve sexual functioning and QOL in women with cancer-related infertility should be a priority of future research.

Keywords

cancer; infertility; survivorship; quality of life; third-party parenting

INTRODUCTION

In 2006, the American Society of Clinical Oncology published guidelines that highlighted lack of research on the impact of infertility in cancer survivors [1]. Parenthood is an important aspect of quality of life (QOL) for many cancer survivors [2,3], but more studies are needed to determine the emotional consequences when this life goal is threatened. An important step in this process is to assess informational needs of cancer survivors with respect to fertility and alternate family-building options, and to determine the impact of this knowledge on long-term QOL and psychosocial adjustment.

Infertility in the general population is an emotionally challenging experience [4], causing distress levels comparable to other major health conditions (i.e., cancer or AIDS) [5]. Research has shown difficulty with menopause, sexuality, and relationship issues within infertile populations [4,6–9]. Cancer-related infertility is purported to mirror the experience observed in non-cancer infertile populations [2,10]. However, it is possible that cancer survivors experience more difficulty adjusting (or a “double trauma” effect) [11]. To date, no study has attempted to compare a non-cancer infertile population with a cohort of cancer-related infertile women, a deficit noted prominently in the literature [2,12].

A possible mitigating factor in the link between cancer-related infertility and emotional response may be adequate information. Understanding the effects of the disease and/or treatment on fertility and potential reproductive options can become increasingly important over time [13]. The relationship between infertility and long-term QOL demonstrates reproductive concerns to be centrally linked to psychosocial outcomes [14]. Many female survivors report insufficient or unavailable information about fertility issues [15,16], but physician knowledge and access to referral networks are key factors in doctor-patient communication on this subject [17,18].

Cancer survivors experiencing ovarian failure and/or loss of their uterus now have the ability to build a family through multiple mechanisms. Third-party parenting options are gaining recognition with enhanced success rates, although a paucity of data exists on the awareness and use of these techniques in cancer survivor populations [1]. By definition, third-party parenting involves the use of a third person to build a family by the donation of gametes (i.e., oocyte [egg], embryo or sperm donation) and/or surrogacy [19]. Unfortunately, there is limited research on how female survivors are addressing their impaired fertility, as well as the psychosocial impact of utilizing fertility preservation [10, 1, 2]. Adoption is another alternative for parenthood. Some research indicates cancer survivors may prefer this method over third-party parenting [20,21] despite the possibility of discrimination due to medical history [19].

Building on existing research, the primary objectives of this study were to (1) describe the emotional and sexual functioning, reproductive concerns, and quality of life of women with cancer-related infertility compared to infertile women without a history of cancer, as well as to test if infertile cancer survivors experience a “double trauma” effect compared to their non-cancer infertile counterparts, 2) identify the extent that cancer survivors experiencing

loss of fertility perceive they have knowledge of and access to potential third-party reproduction options, and (3) test whether knowledge of and access to third-party reproduction options mediate quality of life and emotional functioning among cancer survivors. Empirical measures and exploratory assessment were used to examine this understudied aspect of cancer survivorship research.

METHODS

Participants

Female cancer survivors consisted of gynecologic cancer survivors [GYN] and leukemia/lymphoma/sarcoma cancer survivors treated by Bone Marrow/Stem Cell Transplant [BMT/SCT] who underwent cancer treatment resulting in infertility, but were eligible for third-party parenting techniques. We selected one cancer cohort (gynecologic) with disease directly impacting the reproductive organs compared to another young cancer cohort (BMT/SCT) to determine if site of cancer had any influence on the response to loss of fertility. For this study, cancer-related infertility was defined as loss of the ability to conceive and/or carry a pregnancy, specifically as gynecologic cancer survivors without a uterus but with intact ovaries, or without ovarian function but with an intact uterus; and as BMT/SCT cancer survivors without ovarian function based on FSH determination, but with an intact uterus. The non-cancer infertile group consisted of women with a history of infertility on a wait-list for oocyte donation, a third-party parenting technique.

This was an Institutional Review Board (IRB)-approved study at Memorial Sloan-Kettering Cancer Center (MSKCC) and The Ronald O Perelman and Claudia Cohen Center for Reproductive Medicine (CRM) conducted from 10/06–2/09. Study eligibility criteria for cancer survivors included: 1) history of gynecologic cancer or cancer (leukemia/lymphoma/sarcoma) status post bone marrow or stem cell transplant; 2) no evidence of disease for at least 1 year; 3) no other cancer history; 4) 18–49 years at recruitment; 5) have not started or have not completed childbearing; 6) English speaking; and 7) able to provide informed consent. Non-cancer infertile women study criteria included: 1) no cancer history; 2) 18–49 years at recruitment; 3) history of infertility and on a wait-list for egg (oocyte) donation; 4) have not started or have not completed childbearing; 5) English speaking; and 6) able to provide informed consent.

Study Design and Recruitment

Medical charts were reviewed to identify women who met eligibility criteria. Treating physicians were asked to give permission for letters to be sent to potential subjects. Potential participants were sent introductory letters that described the study co-signed by their treating medical professional and study principal investigator. However, for the BMT/SCT cohort, further discussion occurred between the research team and the treating physicians to ensure that these potential subjects were in ovarian failure due to their cancer treatment and medical history prior to the signing and mailing of the letters. The letters included a phone number for those to call who did not wish any further contact. Potential subjects were approached at medical appointments or by telephone and invited to participate. Upon obtaining consent, all women completed the one-time self-report study survey and data were collected either via telephone or in person in self-report format.

MSKCC site—99 GYN cancer survivors were sent introductory letters. Of the 99 women identified, 22 were unreachable and 20 were deemed ineligible based on study criteria after further discussion with study staff. Fifty-three of 57 eligible women approached for study participation enrolled on the study, but two did not complete the survey; therefore, data was collected for 51 GYN survivors (89% participation rate). For the BMT/SCT arm of the

study, 144 potential childhood and adult cancer survivors were sent letters. Of these 144 women, 25 were unreachable and 31 were deemed ineligible based on study criteria after further discussion with study staff. Of the 88 eligible women reached, 75 enrolled on the study; however, 4 did not complete the survey. Data was collected on 71 BMT/SCT survivors (81% participation rate).

CRM site—In order to receive IRB approval at The Ronald O Perelman and Claudia Cohen Center for Reproductive Medicine, letters could be sent only with the agreement that follow-up contact was conducted directly with participants. It was not permitted to leave messages on answering machines/voicemails. This made contacting women challenging and hindered accrual at this site. Ninety women were identified for possible study participation, but 20 were unreachable and 2 were deemed ineligible after further discussion with study staff. Of 68 women, 4 declined study participation and 13 passively refused (showed interest but did not follow up), for a total of 51 enrolled on study, but one woman did not complete the survey. A total of 50 non-cancer infertile women were assessed (74% participation rate).

Measures

Participants completed a one-time self-report survey including:

The Reproductive Concerns Scale (RCS): The RCS is a 14-item measure assessing the impact of impaired reproductive ability in female cancer survivors. Women rate the relevance of statements regarding possible thoughts and feelings about pregnancy, fertility, and reproduction during the past month on a scale of 0 to 4 (0="not at all bothered", 2="somewhat relevant", 4="very relevant") [14].

2) *The Center for Epidemiologic Studies Depression Scale (CES-D):* This is a 20-item scale assessing depressive symptoms, each rated on a 4-point scale (0="rarely or none of the time", 1="some of the time", 2="occasionally", 3="most of the time"). Scores of 16 or greater on the CES-D suggest depression [22].

3) *The Female Sexual Function Index (FSFI):* This is a 19-item multidimensional scale assessing sexual functioning in women with sub-domains of: desire, arousal, lubrication, orgasm, satisfaction, and pain. A total score ≤26.55 indicates sexual dysfunction [23].

4) *Impact of Events Scale (IES):* This is a 15-item Likert-scale measuring intrusive and avoidant thoughts and behaviors on a 4-point scale (0="not at all", 1="rarely", 3="sometimes", 5="often"). The IES evaluates distress levels in response to a traumatic event. The measure was adapted to assess participants' levels of distress about infertility [12]. Clinical cut-offs were: subclinical (0–8 points), mild (9–25 points), moderate (26–43 points), and severe levels of distress (44+ points) [24,25]. An IES total score, as well as Intrusive and Avoidant subscale scores were calculated.

5) *Menopausal Symptom Checklist:* This is a 36-item scale assessing menopausal symptoms. Women rate how bothered they are by menopausal symptoms over the last 4 weeks on a scale of 0 to 4 (0="not at all bothered", 2="somewhat bothered", 4="very bothered") [26].

6) *The Medical Outcomes SF-12 (SF-12) Health Survey:* The SF-12 is a 12-item self-report measure assessing physical and mental health with eight health domains: physical functioning, role limitations due

to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Patients rate their health on a scale of 1 to 5 (poor to excellent). The domains combine to compose the Physical Component Summary (PCS) and the Mental Component Summary (MCS). A score below 50 indicates below average health status [27–29].

7) *The Abbreviated Dyadic Adjustment Scale (ADAS)* = The DAS is an instrument designed to assess the quality of relationships as perceived by married or cohabiting couples. It is a general measure of satisfaction in relationships. The ADAS is a 7-item short-form designed by Sharpley and colleagues. Normative data suggest a mean ADAS score of 25.6 indicates relationship satisfaction and dyadic adjustment [30,31].

*(Higher scores on the RCS, CES-D, IES, and menopausal symptom checklist indicate elevated symptom/dysfunction levels, while higher scores on the FSFI, SF-12 (PCS/MCS), and ADAS indicate better functioning).

The survey also assessed demographics, cancer history, general medical information, and exploratory items addressing: reproductive informational needs; perception of, utilization of and access to third-party parenting; and health-related concerns (i.e., recurrence, complications, etc.).

Statistical Analysis

Descriptive statistics (frequencies, means, and 95% confidence intervals) were generated to summarize the demographics, medical information, exploratory fertility and third-party reproduction items, and instrument outcomes. Chi square tests assessed differences in the distributions of categorical variables across study arms, while ANOVA (Welch's F, robust to violation of assumption of homogeneity of variance) and follow-up *t* tests assessed differences on continuous variables. Although our goal of summarizing the groups' scores on the instrument outcomes was primarily descriptive in nature, when an overall F was statistically significant ($P<0.05$) we tested for significant differences between the means on the empirical measure for the three groups (GYN, BMT/SCT, and non-cancer infertile) and between the cancer and non-cancer groups in order to determine potential reliable group differences as well as to explore possible patterns of differences among the groups across the instruments. For each measure, the critical *P* values of the follow-up *t* tests were adjusted for multiple comparisons using the Bonferroni approach.

Multivariate analysis of variance (MANOVA) was used to test the "double-trauma" hypothesis, as well as whether knowledge of/access to third-party reproduction options mediated QOL and emotional functioning among cancer survivors. The dependent variables for the "double-trauma" hypothesis were CES-D total, the IES Intrusive and Avoidance subscales, and the SF-12 Physical Component (PCS) and Mental Component Scores (MCS). The independent variable of interest was group (cancer vs. non-cancer), controlling for age (continuous) and education (3 levels). The dependent variables for the "knowledge/access" hypothesis were CES-D total and the IES Intrusive and Avoidance subscales. The independent variables of interest were perceived access to reproductive assistance and perceived need for more information on reproductive options (tested in two separate models), controlling for age (continuous), time since last cancer treatment (continuous), education (3 levels), and cancer group (GYN, BMT/SCT-Adult, and BMT/SCT-Pediatric).

All analyses used the Statistical Package for the Social Sciences (SPSS) (Version 17). Of note, because the BMT/SCT group consisted of adult and childhood survivors, the groups were evaluated on multiple measures simultaneously using multivariate analysis of variance (MANOVA) as well as for individual measures with independent-sample *t*-tests. No significant group differences were found between the adult (diagnosed after the age of 18) and pediatric (diagnosed at the age of 18 or younger) BMT/SCT survivors on any of the psychometric measures. Therefore, statistical analyses contain both subgroups for a combined BMT/SCT group.

RESULTS

Demographics and Medical Characteristics

Table I presents demographic information and medical information by subgroups.

Cancer Diagnosis and Treatment—*A majority of the* GYN cancer survivors had a history of cervical cancer (84%, n=43), and BMT/SCT survivors a history of leukemia or lymphoma (93%, n=66).

Treatment Decision Factors—Approximately one-quarter of GYN cancer survivors (24%, n=12), and 17% (n=12) of BMT/SCT cancer survivors endorsed the item "*fertility played a factor in your decision about cancer treatment*". Participants were also asked if they "*had enough time to complete your childbearing"*; 69% (n=35) of GYN and 76% (n=54) of BMT/SCT cancer survivors responded that they had inadequate time.

Cancer worry—More than two-thirds of GYN (86%, n=44) and BMT/SCT cancer survivors (66%, n=47) expressed concern about recurrence. Participants also rated degree of concern "*that your cancer may come back*" on a scale from 0–10 (0=not at all to 10=very concerned). Despite high percentages of participants reporting concern about recurrence, their degree of concern averaged between 4–5 points, reflective of a moderate intensity of concern.

Empirical Assessment of the Impact of Infertility

Significant group means on the psychometric measures, and 95% confidence intervals are presented in Table II.

Mood—No significant differences were found between groups on the CES-D. Mean scores for all groups ranged from 11–13 points. However, more than one-quarter of participants across all groups scored above the clinical cut-off (16+ points), which suggests depression (GYN: 27.5%, n=14; BMT/SCT: 28.6%, n=20; non-cancer infertile: 32.7%, n=16).

Distress—The IES total score means were significantly different across the three groups (P=0.041). Follow-up tests indicated significant differences between the BMT/SCT group (x=20.41) and non-cancer infertile group means (x=28.24), as well as between the combined cancer and non-cancer infertile group means. A significantly (P=0.005) higher percentage of non-cancer infertile women (59%, n=29) had moderate to severe distress (IES=26 or higher) than GYN (46%, n=23) and BMT/SCT cancer survivors (30%, n=21).

QOL—The groups significantly differed on the PCS (P<0.001). Follow-up pair-wise results indicated that the non-cancer infertile women scored significantly higher than the cancer groups, indicating better physical QOL. No significant group differences were noted on the MCS, but all groups fell below the health status cut-off of 50, indicating below-average mental health status.

Sexual Function—All group FSFI total score means were in the range of sexual dysfunction (≤26.55). Mean FSFI scores were 22.09, 20.27, and 24.09 for the GYN, BMT/SCT, and non-cancer infertile groups, respectively. There were significant differences on the pain and lubrication subscales, with follow-up tests indicating that the cancer survivors experienced more pain and less lubrication than the non-cancer infertile women.

Menopausal Symptoms—No significant group differences were found on the menopausal symptom checklist. Mean scores were 24.88, 25.82, 24.40 for the GYN, BMT/SCT, and non-cancer infertile groups, respectively. Forgetfulness (BMT/SCT: 55%, n=39; GYN: 45%, n=23; non-cancer infertile: 28%, n=14) and vaginal dryness (BMT/SCT: 45%, n=32; GYN: 43%, n=22; non-cancer infertile: 18%, n=9) were reported more frequently among cancer survivors, whereas insomnia (non-cancer infertile: 44%, n=22; BMT/SCT: 37%, n=26; GYN: 22%, n=11) and headaches (non-cancer infertile: 36%, n=18; BMT/SCT: 32%, n=23; GYN: 20%, n=10) were most bothersome for the non-cancer infertile women.

Reproductive Concerns—RCS mean scores were elevated for the cancer survivors (GYN: 26.80, n=50; BMT/SCT: 25.31, n=68) and non-cancer infertile women (27.20, n=49) compared to published values [7,14]. There were no significant group differences.

Relationship Satisfaction—No significant group differences were identified on the ADAS.

Exploratory Items

Parenthood—When asked to "*rate the importance of being a parent to your life*" with a score of 0 (not at all) to 10 (extremely important) GYN cancer survivors had a mean of 8.80 and BMT/SCT survivors had a mean of 8.06. Non-cancer infertile women had a mean of 9.4. A score of 10 reflected parenthood as the highest importance in one's life. Seventy-one percent (n=36) of GYN and 48% (n=34) of BMT/SCT cancer survivors, as well as 66% (n=33) of non-cancer infertile women gave this value for parenthood. Sixty-one percent (n=43) of BMT/SCT and 47% (n=24) of GYN cancer survivors also expressed "*worry about how a cancer diagnosis and treatment may affect their offspring*".

Perceptions and Access to Reproductive Options—Fifty-five percent (n=28) of GYN cancer survivors did not feel they had fertility options compared to 35% (n=25) of the BMT/SCT group (P=0.023). When asked *"if you wanted to talk about reproductive assistance, do you know where to go or with whom to speak?"* 73% (n=52) of BMT/SCT cancer survivors gave a positive response compared to 49% (n=25) of GYN cancer group (P=0.013). Sixty-three percent (n=32) of GYN and 75% (n=53) of BMT/SCT cancer survivors indicated *"it would be helpful (or was helpful) to speak with a fertility counselor or reproductive specialist".* However, only approximately one-third of cancer survivors (GYN: 33%, n=17; BMT/SCT: 38%, n=27) had ever spoken with one. At assessment, only 18% (n=9) of GYN and 24% (n=17) of BMT/SCT cancer survivors had used assisted reproductive techniques.

Infertility Communication and Disclosure—Approximately two-thirds of the study sample indicated being comfortable discussing their reproductive concerns, as well as reporting a positive or supportive response by others to their infertility.

Third-party parenting options—Almost all cancer survivors (GYN: 98%, n=50; BMT/SCT: 94%, n=67) were familiar with surrogacy, and a large proportion had heard of oocyte retrieval (GYN: 72.5%, n=37; BMT/SCT: 82%, n=58) and oocyte donation (GYN: 74.5%, n=38; BMT/SCT: 84.5%, n=60). When queried if oocyte retrieval was thought about or

considered, 31% (n=16) of GYN and 39% (n=28) of BMT/SCT cancer survivors indicated this as a consideration. However, 61% (n=31) of GYN and 51% (n=36) of BMT/SCT cancer survivors considered oocyte donation. Surrogacy was also viewed as a viable option by 53% (n=27) of GYN and 66% (n=47) of BMT/SCT cancer survivors. Willingness to explore alternatives to childbirth, such as adoption or foster parenting was acceptable to 71% (n=36) of GYN and 87% (n=62) of BMT/SCT cancer survivors and 84% (n=42) of non-cancer infertile women. However, concern about trying to adopt as a cancer survivor was an issue for 42% (n=30) of BMT/SCT and 35% (n=18) of GYN cancer survivors. Participants also ranked the acceptability of reproductive techniques (egg donation, surrogacy, adoption, and foster parenting) (Table III).

Multivariate Comparisons

Comparisons of Cancer and Non-Cancer Infertile Women with Respect to Depression, Distress, and QOL: The Double-Trauma Hypothesis—ANOVA results indicated a significant group effect ($F(5,146)=4.22$, $P<0.01$); however, examination of group univariate ANOVAs and marginal means of each of the 5 dependent variables (Table IV) revealed that the non-cancer infertile group generally had levels of depression and distress comparable to the women with cancer, but significantly better physical QOL (SF-12 PCS).

Comparison of Effects of Access to and Knowledge of Third-Party Reproductive Options Among Cancer Survivors—The MANOVA model failed to find a significant effect of perceived access to third-party reproduction options on depression and distress among women with cancer-related infertility ($F(3,96)=.90$, $P=0.44$). A second MANOVA model did, however, find a significant impact of knowledge of third-party reproductive options on depression and distress levels ($F(3,97)=4.62$, $P<0.01$). Examination of marginal means (Table IV) revealed that women with perceived need for more information had significantly higher depression and avoidance scores than women reporting no need for more information about reproductive options.

DISCUSSION

The overall study aim was to investigate the needs of cancer-related infertile women in comparison to non-cancer infertile women and explore survivors' knowledge and perception of family-building alternatives. Our initial question was "Will cancer survivors demonstrate a double-trauma response [32] to loss of fertility?" The study findings are more supportive of the theory that cancer-related infertility emotionally mirrors the experience of non-cancer infertile women. No significant differences on measurements of mood, reproductive concerns, and mental health QOL were identified between infertile groups (cancer vs. non-cancer), yet all scores fell below published data, indicating poor adjustment to infertility regardless of etiology. Reproductive concerns were reported by the majority of women, and parenthood was rated as highly important, regardless of the etiology of infertility. Greater than 25% of the total sample scored in the range suggestive of depression, confirming existing research.

If a double-trauma effect was to occur for cancer survivors, it would appear to be associated with physical effects, which was supported in both univariate and multivariate analyses. Group differences were seen for sexual functioning (FSFI) and physical health QOL (SF-12) between cancer and non-cancer infertile women. Cancer survivors demonstrated greater sexual dysfunction and lower physical QOL than non-cancer infertile women. Although the physical QOL scores were close to those reported in the general population, the cancer survivors did demonstrate lower physical QOL scores when compared to the non-cancer

infertile group. This may reflect treatment sequelae particularly in the BMT/SCT group; however, these differences could also be reflective of the women in the non-cancer infertile group who are trying to facilitate conception by optimizing health and fitness. Despite the differences detected between infertile groups on the FSFI, all women exhibited poor sexual functioning (≤26.55), consistent with literature on other cancer [6–9] and non-cancer infertile populations [4].

The infertility literature describes an adaptive response occurring over time as women focus on new life goals when conception is unsuccessful [33]. The nature of cancer-related infertility in addition to time since treatment (at least 1 yr +) may have facilitated emotional adjustment to reproductive loss in our sample. Contrastingly, the CRMI infertile women are in the midst of their medical crisis, infertility, and are actively awaiting oocyte donation. For those who persist in attempts for conception despite lack of success, anxiety and depression can worsen [33] due to the constant threat of failure [33] and prolonged duration of treatment (34,35). This may also offer explanation about the higher degree of distress and stress-related menopausal symptoms (headaches and insomnia) reported by women in the non-cancer infertile group.

We also sought to answer the question “Do cancer survivors have knowledge of and access to alternate family-building options?” Overall, cancer survivors felt comfortable speaking with others about reproductive concerns and were in favor of speaking with a reproductive specialist, but only approximately one-third sought consultation. Even though the majority of the sample reported knowledge of alternate family-building options (surrogacy, oocyte retrieval, and oocyte donation), adoption was viewed as the most acceptable option, despite the worry of trying to adopt as a cancer survivor seen in one-third of the sample. Our findings support the existing literature, which notes that among cancer survivors, adoption is viewed as more acceptable than gamete donation [20,21,36], although potential concerns about discrimination during the adoption process exist [19]. Multivariate analysis revealed perceived access did not impact emotional response, although knowledge of third-party reproduction options did influence mood and distress levels. Those who indicated an unmet need regarding information about reproductive options and issues appeared to have a higher disturbance of mood and avoidance coping. However, the directionality of these results is unclear—whether lack of information causes distress or distressed women avoid seeking information.

Differences Noted Between Cancer Groups

More of the GYN cancer survivors (71%) indicated parenthood as being of highest importance (48% for BMT/SCT survivors) in their lives. In general, cancer survivors appeared more knowledgeable about surrogacy than the reproductive options of oocyte egg) retrieval or oocyte donation. However, when queried about which option was *thought about or considered,* oocyte donation was considered by at least half of cancer survivors. For perceived acceptability, adoption was endorsed as the most acceptable alternate family-building option in both cancer survivor cohorts (Table III). Even though approximately two-thirds of cancer survivors reported it would be helpful to speak with a reproductive specialist, the GYN cancer survivors expressed a greater need for information about where to go or with whom to speak about these issues. This finding may be connected with their positive endorsement (or perception) of not having fertility options, despite availability of reproductive alternatives.

This could also reflect physician-patient communication differences in approaches between those patients being treated for BMT/SCT to those being treated for gynecologic cancer due to site of disease. It is also possible that age and marital status could contribute to whether or not patients had sought reproductive options or viewed them as acceptable. Seventy-three

percent of the GYN cancer survivors in our study were married, with a mean age of 38; however, the mean age of the BMT/SCT survivors was 33, with 48% being single and 44% married. However, in a recent study by Zebrack and colleagues, younger patients as well as those who were unmarried reported significantly greater unmet needs in regards to information about infertility treatment [37].

Limitations

One limitation of the current study involves sample selection, which was contingent on all infertile women being appropriate candidates for third-party parenting options. As such, we selected cancer survivors eligible for third-party parenting techniques in comparison to infertile women awaiting oocyte donation. In retrospect, the ideal infertile comparison group may have been infertile women with no plans for future fertility treatment (and off treatment for at least 1 year). This may not have been feasible due to challenges identified in the infertility literature, including loss of contact when treatment is no longer sought and complexity in determining when treatment has truly ceased [33–35]. Additionally, for IRB approval, our cancer survivors needed to be at least 1 year from treatment; it is unclear if we had the opportunity to assess and measure the distress levels of survivors closer to their initial diagnosis in real time if a different emotional response would have been detected, as has been suggested in retrospective studies [13,38].

Conclusions

Loss of fertility is an emotionally difficulty experience for women, regardless of the cause, but for those surviving cancer it may be connected to the physical ramifications of cancer treatment. Additionally, cancer survivors would welcome the opportunity to speak with reproductive specialists but may need guidance in identifying resources. Although third-party parenting offers new methods to build families in survivorship, cancer survivors viewed adoption as the most acceptable option. Future research should explore what factors or beliefs (i.e., cultural, societal, religious) may influence cancer survivors' willingness to consider reproductive medicine techniques. In our sample, few cancer survivors utilized reproductive medicine techniques (GYN, 18%; BMT/SCT, 24%); as a result, an adequate investigation about the impact of health policy issues (i.e., financial, insurance coverage) was not possible. Future research should attempt to clarify the influence of these issues on family-building options in cancer survivors.

Future directions should consider targeted interventions to increase knowledge about reproductive options and assist women pursuing parenthood in cancer survivorship. Our findings also support the need for the development of intervention studies to improve sexual functioning and QOL in women coping with cancer-related infertility. Prospective studies investigating these issues is also greatly needed to examine the psychosocial aspects and informational needs of cancer-related infertile women *throughout the continuum of care* using empirical measures since much of the existing literature is retrospective in nature.

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Table I

Demographic Information and Medical Characteristics

		GYN Cancer Survivors (n=51)	BMT/SCT Survivors (n=71)	Non-Cancer Infertile Women (n=50)	P Value
Mean Age, years	Study Assessment	38.43 (range, 22–49)	32.92 (range, 18–49)	40.18 (range, 28–46)	<.01
Mean Age, years	Cancer Diagnosis	34.78 (range, 21–46)	23.13 (range, 4–45)	No cancer diagnosis	<.01
Marital Status:	Single	20%(n=10)	48%(n=34)	4%(n=2)	<.01
	Married or living w/someone	73%(n=37)	44%(n=31)	94%(n=47)	
	Separated/Divorced	8%(n=4)	8%(n=6)	--------	
	Widowed	--------	--------	--------	
Education:	Less than 11th grade		1%(n=1)	------	<.01
	HS grad/GED	14%(n=7)	10%(n=7)	------	
	Some college/college grad	51%(n=26)	55%(n=39)	60%(n=30)	
	Graduate School or higher	35%(n=18)	34%(n=24)	40%(n=20)	
Race	White	88%(n= 45)	87%(n=62)	96%(n= 48)	ns
	Black	8%(n=4)	3%(n=2)	2%(n=1)	
	Asian/Pacific	2%(n=1)	7%(n=5)	2%(n=1)	
	Other	2%(n=1)	3%(n=2)	--------	
Ethnicity	Non-Hispanic	88%(n=45)	87%(n=62)	90%(n=45)	ns
	Hispanic	12%(n=6)	13%(n=9)	10%(n=5)	
Hormonal Supplements	Yes	22%(n=11)	62%(n=44)	32%(n=16)	<.01
	No	78%(n=40)	38%(n=27)	68%(n=34)	
Medications	Yes	27.5%(n=14)	65%(n=46)	24%(n=12)	<.01
	No	72.5%(n=37)	35%(n=25)	76%(n=38)	
Time Since Diagnosis		Mean=3.76 years (range, 1–11)	Mean=9.66 years (range, 2–29)		<.01
Cancer Type		Cervical 84%(n=43)	Leukemia 45%(n=32)		---
		Ovarian 2%(n=1)	Lymphoma 48%(n=34)		
		Endo/uterine 6%(n=3)	Sarcomas 7%(n=5)		

		GYN Cancer Survivors (n=51)	BMT/SCT Survivors (n=71)	Non-Cancer Infertile Women (n=50)	P Value
		GTD 8%(n=4)	(Ewings sarcoma or Rhabdomyosarcoma)		
Time Since		Mean=41.73 months	Mean=95.37 months		<.01
Treatment		(3.48 years)	(7.95 years)		
Treatment	Surgery	88%(n=45)	31%(n=22)		<.01
	Radiation	37%(n=19)	85%(n=60)		<.01
	Chemo	41%(n=21)	99%(n=70)		<.01
	BMT	----------	100%(n=71)		----

*The p-values for categorical variables are from Fisher's exact tests. The p-values for continuous variables are from Kruskal-Wallis tests for variables with data from all three groups and from Wilcoxon rank-sum tests for variables with data from only two groups. There was no significant difference in education between the GYN and BMT/SCT survivors in a follow-up Fisher's exact test that included only these two groups.

Table II

Means of Continuous Measures

	GYN			BMT/SCT			Non-Cancer			P-value*
By Group	**Total n**	**Mean**	**95% CI**	**Total n**	**Mean**	**95%CI**	**Total n**	**Mean**	**95% CI**	
Age	51	38.43[a]	(36.75–40.11)	71	32.91[ab]	(30.94–34.90)	50	40.18[b#]	(39.01–41.35)	0.000
Rate the importance of being a parent to your life	51	8.80	(8.14–9.47)	69	8.06[a]	(7.43–8.68)	49	9.41[a#]	(9.13–9.68)	0.000
(O: not at all to 10 very concerned)										
CES-D Total Score (Depressive Symptoms)	51	11.32	(8.51–14.13)	70	12.18	(9.71–14.65)	49	13.15	(10.30–15.99)	0.658
(16+ suggestive of depression)										
FSFI Total (Sexual Functioning)	49	22.09	(19.66–24.51)	66	20.27	(17.60–22.93)	47	24.09	(21.45–26.74)	0.130
Normal Range (>26.55), Norms (30.75)										
FSFI Desire Subscale	51	3.22	(2.82–3.62)	70	3.15	(2.84–3.47)	49	3.34	(3.02–3.67)	0.702
Norms (4.28)										
FSFI Arousal Subscale	51	3.72	(3.20–4.23)	70	3.02	(2.52–3.52)	49	3.69	(3.19–4.20)	0.093
Norms (5.08)										
FSFI Lubrication Subscale	51	3.49	(3.08–3.91)	69	3.24[a]	(2.70–3.79)	49	4.23[a#]	(3.66–4.81)	0.037
Norms (5.45)										
FSFI Orgasm Subscale	50	4.11	(3.58–4.63)	69	3.17	(2.60–3.73)	48	4.08	(3.46–4.69)	0.032
Norms (5.05)										
FSFI Satisfaction Subscale	51	3.76	(3.21–4.32)	70	3.49	(2.97–4.01)	49	3.97	(3.49–4.45)	0.407
Norms (5.04)										
FSFI Pain Subscale	50	3.39[a]	(2.97–3.81)	66	3.52[b]	(2.89–4.15)	48	4.58[ab#]	(3.92–5.23)	0.010
Norms (5.51)										
IES Total (Distress about Infertility)	50	24.48	(19.35–29.61)	71	20.41[a]	(16.15–24.66)	49	28.24[a#]	(23.87–32.62)	0.041
Moderate to Severe (26+)										
IES Intrusive Subscale	51	10.69	(8.32–13.05)	71	9.46[a]	(7.35–11.58)	49	14.88[a#]	(12.28–17.47)	0.006
IES Avoidance Subscale	50	13.90	(10.90–16.90)	71	10.94	(8.58–13.31)	49	13.37	(11.01–15.72)	0.215
Menopausal Symptom Checklist Total	50	24.88	(20.16–29.61)	71	25.82	(20.61–31.03)	49	24.40	(18.94–29.86)	0.929

	GYN			BMT/SCT			Non-Cancer			P-value*
By Group	**Total n**	**Mean**	**95% CI**	**Total n**	**Mean**	**95%CI**	**Total n**	**Mean**	**95% CI**	
SF-12 PCS (Physical Component Summary)	46	51.39[a]	(48.64–54.14)	65	49.55[b]	(47.23–51.87)	47	56.76[ab#]	(55.48–58.05)	0.000
SF-12 MCS (Mental Component Summary)	46	46.58	(43.03–50.13)	65	47.72	(44.63–50.81)	47	44.63	(41.35–47.90)	0.387
ADAS Total Score (Relationship Satisfaction)	41	24.54	(22.58–26.49)	45	25.71	(24.21–27.21)	48	25.54	(24.23–26.86)	0.606
Reproductive Concerns Scale Total	50	26.80	(23.39–30.21)	68	25.31	(22.71–27.91)	49	27.20	(24.92–29.49)	0.539

*P values are based on the F statistic from the Welch test, an ANOVA alternative that is robust to violation of assumption of homogeneity of variance among groups.

NOTE: Means within a row with identical superscripts had significant overall ANOVAs and were significantly different at $P<.05$ by pair-wise t-tests with Bonferroni adjustment;

#denotes the cancer groups' mean scores significantly differed from means of the non-cancer group.

Higher scores on RCS, CES-D, IES, and Menopausal SCL indicate elevated symptom/dysfunction levels, higher scores on the FSFI, PCS, MCS, and ADAS indicate better functioning.

Table III

Rank Order of Acceptability of Reproductive Techniques

Most Acceptable				*Least Acceptable*		
Gynecologic (n=51)	**Rank #1**	**Adoption**	**(47%, n=24)**	**Rank #4**	**Egg Donation**	**(35%, n=18)**
		Surrogacy	(31%, n=16)		Foster child	(29%, n=15)
		Egg donation	(18%, n=9)		Surrogacy	(16%, n=8)
		Foster child	(4%, n=2)		Adoption	(10%, n=5)
BMT/SCT (n=71)	Rank #1	Adoption	(41%, n=29)	Rank #4	Surrogacy	(39%, n=28)
		Egg donation	(37%, n=26)		Foster child	(39%, n=28)
		Surrogacy	(13%, n=9)		Egg donation	(21%, n=15)
		Foster child	(9%, n=6)		Adoption	———
Non-cancer Infertile (n=50)	Rank #1	Egg donation	(94%, n=47)	Rank #4	Foster child	(62%, n=31)
		Adoption	(8%, n=4)		Surrogacy	(26%, n=13)
		Surrogacy	(2%, n=1)		Egg donation	(2%, n=1)
		Foster child	--------		Adoption	———

*Percentages may not add to 100% due to missing data and/or multiple responses to certain items.

Table IV

Adjusted Means for Multivariate Hypothesis Tests

Hypothesis: Cancer survivors with infertility will show "Double Trauma" of having both cancer and infertility compared to non- cancer infertile women.					
				95% Confidence Interval	
Dependent Variables	**All Cancer vs. NON-CANCER INFERTILE WOMEN**	**Mean[a]**	**Std. Error**	**Lower Bound**	**Upper Bound**
CES-D Total (Depressive Symptoms)	Cancer	12.20	.997	10.226	14.165
	Non-Cancer	11.72	2.252	7.266	16.163
IES Intrusive (Distress, Intrusive Thoughts/Behaviors)	Cancer	9.83*	.881	8.091	11.573
	Non-Cancer	13.75*	1.990	9.820	17.685
IES Avoidance (Distress, Avoidant Thoughts/Behaviors)	Cancer	12.02	.959	10.124	13.912
	Non-Cancer	12.25	2.165	7.975	16.532
SF-12 PCS (Physical Health Quality of Life)	Cancer	50.10**	.817	48.488	51.715
	Non-Cancer	56.99**	1.845	53.342	60.632
SF-12 MCS (Mental Health Quality of Life)	Cancer	46.60	1.171	44.287	48.913
	Non-Cancer	46.89	2.644	41.662	52.112
Hypothesis: Infertile cancer survivors with perceived access to reproductive assistance will have less depression and distress than those without perceived access.					
				95% Confidence Interval	
Dependent Variables	**If you wanted to talk about rep. assist, do you know where to go or whom to speak about this?[c]**	**Mean[b]**	**Std. Error**	**Lower Bound**	**Upper Bound**
CES-D Total (Depressive Symptoms)	No	13.75	2.062	9.663	17.845
	Yes	10.84	1.425	8.009	13.665
IES Intrusive (Distress, Intrusive Thoughts/Behaviors)	No	11.43	1.740	7.980	14.888
	Yes	8.17	1.203	5.782	10.558
IES Avoidance (Distress, Avoidant Thoughts/Behaviors)	No	13.36	2.046	9.303	17.424
	Yes	9.45	1.415	6.643	12.258
Hypothesis: Infertile cancer survivors with perceived need for more information about reproductive assistance will have greater depression and distress than those who feel their informational needs are met.					

Hypothesis: Cancer survivors with infertility will show "Double Trauma" of having both cancer and infertility compared to non- cancer infertile women.					
				95% Confidence Interval	
Dependent Variables	**All Cancer vs. NON-CANCER INFERTILE WOMEN**	**Mean[a]**	**Std. Error**	**Lower Bound**	**Upper Bound**

				95% Confidence Interval	
Dependent Variables	**Do you feel you need more info on options and issues?[d]**	**Mean[b]**	**Std. Error**	**Lower Bound**	**Upper Bound**
CES-D Total (Depressive Symptoms)	No	9.41**	1.560	6.313	12.503
	Yes	14.60**	1.424	11.776	17.428
IES Intrusive (Distress, Intrusive Thoughts/Behaviors)	No	8.13*	1.369	5.413	10.845
	Yes	11.83*	1.250	9.347	14.306
IES Avoidance (Distress, Avoidant Thoughts/Behaviors)	No	8.72**	1.541	5.660	11.776
	Yes	14.41**	1.407	11.619	17.202

[a] Least-squares mean from MANOVA model including age at assessment and education.

[b] Least-squares mean from MANOVA model including age at assessment, years since last cancer treatment, education, and cancer group (GYN, BMT-adult, and BMT-Pediatric).

[c] The interaction between cancer group and perceived access to reproductive assistance was not statistically significant.

[d] The interaction between cancer group and perceived need for more information about reproductive assistance was not statistically significant.

** Significantly different at $p < 0.05$, after Bonferroni correction for multiple comparisons.