Fertility Preservation Preferences and Perspectives Among Adult Male Survivors of Pediatric Cancer and Their Parents

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Purpose: In this study, we set out to determine the preferences, concerns, and attitudes toward fertility preservation of adult male survivors of pediatric cancer and their parents.

Methods: We conducted 3 focus groups with a total of 15 male survivors of pediatric cancer (age at diagnosis: mean=14, range: 10–20; age at study: mean=35, range: 25–47) and 2 groups with a total of 7 parents of survivors. Grounded theory methodology was used for the identification and analysis of recurrent themes expressed by survivors and their parents in the course of focus group discussions.

Results: Themes most frequently expressed by survivors included concern regarding long-term treatment effects and a retrospective desire for fertility impairment to have been discussed when they were originally diagnosed with cancer. Parental themes included the same hindsight desire, as well as reliance upon the treating oncologist for direction in selecting the course of treatment, and an acknowledgment that input from a specialist in fertility preservation would have been beneficial.

Conclusions: Although future reproductive potential was not consistently reported as a source of apprehension when diagnosed with cancer, both survivors and their parents noted it to be a paramount concern later in life. Parents and survivors both reported that fertility preservation discussions should be routinely incorporated in the clinical context of a pediatric cancer diagnosis.

Keywords: cancer survivorship, fertility preservation, oncofertility, pediatric oncology, sperm cryopreservation

MODERN DAY ADVANCEMENTS in cancer treatment have led to a gradual decline in pediatric cancer mortality rates, with reported 5-year survival rates now exceeding 80% across all age groups under age 20.¹ As an increasing number of pediatric cancer patients are expected to survive into adulthood, more emphasis has been placed on the importance of future quality of life among these cancer survivors. Chief among the many life-altering effects endured by survivors of pediatric cancer is the issue of potential infertility. Cancer treatment protocols such as chemotherapy and radiation therapy are known to be highly destructive to gonadal tissue in an agent- and dose-dependent manner and may result in severe fertility impairment, which can sometimes be permanent.^{2,3} Studies of spermatogenesis in long-term male

pediatric cancer survivors have demonstrated evidence of persistent azoospermia or severe oligospermia in up to 24% of survivors.⁴ Similarly, investigations of long-term pregnancy outcomes for these survivors have evidenced a diminished fertility potential, as a cohort of over 6,000 male pediatric cancer survivors were found to be about half as likely as their healthy siblings to successfully father a child.⁵

In pubertal male patients facing cancer treatment, the potential for future biological paternity can oftentimes be preserved through the cryopreservation of semen samples prior to the onset of treatment. Cryopreserved sperm can be stored and later utilized in assisted reproductive techniques, such as intrauterine insemination or *in vitro* fertilization with intracytoplasmic sperm injection (IVF-ICSI), in order to

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achieve a pregnancy. There has been extensive documentation throughout the medical literature of successful pregnancies resulting from the use of sperm cryopreserved in advance of oncologic treatment for the purposes of fertility preservation.^{6–8} Studies have also shown that up to 86% of pediatric cancer patients referred for pre-treatment sperm banking were able to produce semen samples viable for cryopreservation, with successful cryopreservation reported in patients as young as 12 years old.^{9–11} Furthermore, clinical pregnancy rates from IVF-ICSI using pre-treatment cryopreserved sperm from cancer patients are as high as 56.8%.¹²

In 2006, the American Society of Clinical Oncology (ASCO) issued formal recommendations for fertility preservation in cancer patients.¹³ These recommendations state that oncologists should discuss the issue of fertility preservation with patients shortly after the time of initial cancer diagnosis, and that a referral to a fertility preservation specialist should be made as soon as possible, if appropriate. Concerning males specifically, the recommendations strongly advise that sperm cryopreservation should be undertaken in all eligible cases, and that every effort should be made to ensure the collection of sperm prior to the initiation of treatment. In 2011, a nationwide survey of pediatric oncologists was published that ascertained practitioner attitudes and practice patterns in the wake of the ASCO recommendations' release. The study revealed that although 86% of responding pediatric oncologists agreed with the recommendation to refer all pubertal males to a physician who specializes in fertility preservation care in advance of oncologic treatment, merely 46% of respondents reported actually doing so more than half of the time.¹⁴ In addition, only 44% reported familiarity with the ASCO recommendations, and only 39% used the recommendations with more than half of their patients.¹⁴

A subsequent study sought to identify factors that influence the discussion of fertility preservation in the context of pediatric cancer care by collecting qualitative data from interviews with pediatric oncologists.¹⁵ These interviews shed light on pediatric oncologists' perceptions of patient and parent attitudes towards fertility preservation discussions. Most respondents described discussions of fertility as being directed toward the parents and not the patient, unless the patient was over age 18. Half of the pediatric oncologists believed that parents were either uncomfortable with discussions of fertility or were so focused on the survival of their child that they did not wish to discuss fertility. The physicians reported monitoring body language cues from the parents to gauge discomfort levels and electing to end fertility preservation discussions if the parents seemed overwhelmed or disinterested. With regard to their perception of patients' receptiveness to discussing fertility preservation, the pediatric oncologists believed that about half of their male patients were embarrassed by the dialogue and were not actively considering future paternity, making them less receptive to a discussion about fertility preservation. These provider perceptions may influence practice patterns, as only 50% of respondents in the study reported providing referrals to a fertility specialist.¹⁵

Given the importance of patient and parental viewpoints on fertility preservation efforts in the pediatric cancer population, as well as the relative dearth of basic research to date in this area, a patient-centered, qualitative methodological

approach represents the next logical step needed to provide a formative base of information. Grounded theory is a qualitative approach used to discover and conceptualize latent social phenomena as a means of developing a greater understanding that is "grounded in" the data themselves. This approach is especially apropos when one is attempting to observe and explain an underlying phenomenon rather than test or validate existing assumptions. We therefore set out in the present study to use grounded theory to qualitatively examine the attitudes held by adult-aged male survivors of pediatric cancer and their parents regarding fertility preservation and sperm cryopreservation. Through the identification of barriers and misconceptions that can complicate fertility preservation discussions, we sought to improve understanding of the preferences and viewpoints among these survivors and their families, which may ultimately enhance future pediatric fertility preservation efforts.

Methods

Study population

Adult-aged male survivors of pediatric cancer and their parents were identified from an institutional cancer registry and consented to participate in separate moderated focus group discussions. By our inclusion criteria, male survivors aged 18–55 years old at study and diagnosed with cancer while aged 10–21 years old were eligible to participate. Survivors were permitted to participate independent of whether or not their parents participated.

Study design

The focus groups were led by trained moderators who adhered to a semi-structured guide intended to elicit participants' past and present attitudes towards, preferences for, and concerns regarding fertility preservation for pediatric cancer patients. Generalized prompts were employed to facilitate open-ended discussion among the groups about topics such as fertility, sexual health, and fertility preservation. The primary objective of our study was to identify themes in the attitudes and viewpoints of our study population with regard to fertility preservation in the context of pediatric oncologic diagnosis. The requisite institutional review board approval was obtained from our institution for this study.

Data analysis

All discussion sessions were audio-recorded, transcribed, and de-identified prior to content analysis. Grounded theory analytical methodology¹⁶ was utilized to systematically identify and organize relevant themes recurring throughout the focus group discussions. By this process, one transcript was first read in full by at least two reviewers to obtain a general sense of the participants' experiences. Next, reviewers proceeded to establish coding rules and then independently and exhaustively assigned codes to words, phrases, and text passages of the same transcript as themes emerged. From this exploratory coding exercise, referred to as *open coding*, coders examined and broke down transcript content into thematic sub-units of meaning. Next, code definitions were created and an initial codebook was developed. Two additional coders were trained using this codebook. These

codes were thematically applied to the remaining transcripts, a process referred to as *axial/selective coding*, and data saturation, or the degree to which no new codes are applied,¹⁷ was achieved. Analysis was performed using the qualitative research software NVivo v9 (QSR International, Burlington, MA).

Results

Participants

Fifteen adult-aged male pediatric cancer survivors participated in one of three separate survivor focus groups. Seven parents of survivors participated in one of two parent focus groups that were held separately. At the time of the study, survivors' ages ranged from 25–47 years old, with a mean age of 35 (median age = 34). The survivors' mean age at the time of cancer diagnosis was 14 years old (median age = 14), with an overall range of 10–20, while the mean time elapsed since diagnosis was 22 years (median elapsed time = 20 years; range: 9–35 years). The most common cancer diagnosis among the survivors was Hodgkin lymphoma (57%). The majority of the survivors were Caucasian (86%), college graduates (64%), and married (71%); 39% reported having children.

Thematic content

In total, 28 discrete themes were identified from analysis of the survivors' discussions, with 95% inter-rater agreement

achieved between coders, while 24 themes surfaced from amongst the parents' discussions, with 97% inter-rater agreement achieved (Figs. 1–3).

Survivor focus groups. A complete listing of the 28 survivor themes appears in Figure 1, along with representation of their relative frequency throughout the survivors' discussions. The most prominent theme expressed by survivors was regret that the issue of potentially compromised fertility had not been adequately addressed at the time of cancer diagnosis. Although many survivors did not fully recognize the issue of fertility at that time, in hindsight they uniformly acknowledged that the true impact of potential fertility impairment eventually emerged later in life as they dealt with issues of relationships and family planning in adulthood. They also noted that it would have been impractical to expect themselves or their parents to bring up fertility at the time, and felt that responsibility to raise the issue had rested with their providers. Participant quotes illustrative of this theme are noted in Table 1. The other most frequently coded theme expressed by survivors was anxiety about the long-term effects of cancer treatment in general (Table 1).

Parent focus groups. The 24 coded parent themes are listed in Figure 2, along with relative percent coverage throughout the parental focus groups' discussions. As with the survivor groups, hindsight regret that fertility

FIG. 1. Coded themes from survivor focus groups. *Note.* Relative percent coverage represents the frequency of thematic occurrence throughout discussions with survivors.

FIG. 2. Coded themes from parent focus groups. *Note.* Relative percent coverage represents the frequency of thematic occurrence throughout discussions with parents.

was not addressed at diagnosis again emerged as the most prominent theme. However, in the parent groups, this regret was accompanied by a strong sense of guilt that they had not thought to raise the issue in treatment discussions. Representative quotes of this parental theme appear in Table 2.

Additionally, parents frequently expressed a deference to the treating oncologist throughout the decision-making process regarding matters of care and treatment, including fertility preservation; they also wished that the oncologist had raised the issue of fertility concerns for them (Table 2). Also among the most recurrent parental themes was a

FIG. 3. Comparison of themes expressed by survivors and parents. *Note.* Shared themes appear down the center of the diagram, while unique themes appear to the side. Box size represents relative frequency of appearance for each theme throughout focus group discussions.

TABLE 1. REPRESENTATIVE QUOTES FROM SURVIVOR FOCUS GROUPS

Theme	Quotes
Regret	<p>“I see [fertility] is important to me now.”</p> <p>“Marriages break up over this issue frequently... You know, it’s a huge thing in our lives.”</p> <p>“I wish that these things had been brought up by my doctor, but I think they weren’t because at the time people were generally more conservative about how people would react to these sensitive issues. It’s really weird ’cause you are talking to a 13 year old about having kids. It’s a strange topic but I think it’s incredibly important, especially with kids even younger.”</p> <p>“I was only 16 years old, and you just weren’t that concerned about it at the time. Looking back I kind of wish they had set aside a time or an appointment, more than just like 2 minutes.”</p> <p>“My parents, conservative parents, don’t really know how to bring up that topic, but I wish the doctor would have brought it up with me.”</p>
Long-term effects of cancer treatment	<p>“I think an issue is that so much [of] cancer treatment is cutting-edge or experimental to some degree, and so...it’s [like] a new drug. You never know what the long-term effects are going to be until 10 years have [gone] by and enough people have taken that drug.”</p> <p>“The doc is so focused on the immediate cure that I think [the patient and parents] just accept whatever they say is the course of treatment right off the bat. I just don’t feel like there is ever a moment to pause, really, and say, ‘...There’s a good chance this is going to save your life, but these are the long-term effects, or some other quality of life things you may want to consider.’”</p>

desire to have had a fertility specialist involved to address the issue of fertility preservation alongside the oncologist (Table 2). Lastly, parents often expressed that they interpreted provider willingness to consider fertility preservation as a sign of hope for their child’s long-term survival (Table 2).

Discussion

Fatherhood is known to be an important issue among young male cancer survivors. Schover et al. reported that over half of men aged 14 to 40 with a recent cancer diagnosis desire future paternity, including 75% of men who

TABLE 2. REPRESENTATIVE QUOTES FROM PARENT FOCUS GROUPS

Theme	Quotes
Regret	<p>“I should have protected him.”</p> <p>“I did nothing, and then I lived with torment for years.”</p> <p>“I really beat myself up with guilt [in the time since].”</p> <p>“This should have been part of the information they gave us.”</p> <p>“Would we have been adverse to it? Absolutely not.”</p> <p>Mother to father: “See, why didn’t you open your mouth? Why didn’t you just say something?”</p> <p>Father: “It was the last thing on our minds.”</p> <p>Mother: “Not the last thing on his mind probably.”</p>
Deference to physician	<p>“When we bring a child into the hospital, this is our first experience, we know virtually nothing. The doctor communicates everything to us that we know.”</p> <p>“We just basically took Dr.—’s word that it wasn’t an option for our son, so it was a moot point at that time.”</p> <p>“We thought [the doctor] was God.”</p> <p>“If they had said something about [fertility preservation], we would have thought more about it.”</p> <p>“I wanted someone all along to bring [fertility] up.”</p> <p>“I was just too self conscious to ask about it, and I just kept thinking, ‘The doctor will say something—he’ll say something if...’ I just felt awkward.”</p> <p>“I was so embarrassed. I didn’t know how to bring it up to the doctor.”</p>
Desire for fertility specialist involvement	<p>“I would have liked someone from your expertise to speak to our son and my husband and I, rather than the oncologist...I think if you heard it from a different person, your ears would [perk] up.”</p> <p>“I would like to see that person and the oncologist together.”</p> <p>“Would have liked to have had experts to come in and talk to us as a family.”</p>
Fertility discussion as hope	<p>“Someone is looking beyond the big problem sitting right here in front of us and showing us there’s light at the end of the tunnel.”</p> <p>“There is hope...if there’s fertility discussed...then you’re saying to me that he could be in that...survival [group].”</p> <p>“You’re giving that child a future.”</p>

were childless at the time of diagnosis.¹⁸ In fact, 24% of childless male survivors in the study expressed that their experiences with cancer actually increased their wish to have children.¹⁸ Despite the relevancy and efficacy of sperm cryopreservation technology, studies have shown that as few as 17% of newly-diagnosed male cancer patients under age 30 utilize cryopreservation.¹⁹ Patients not having been informed about the option has been retrospectively identified as the most common barrier to sperm banking in this situation.¹⁶ As the provider's perception of the patient's preferences plays a prominent part in shaping fertility preservation discussions, an understanding of patient and parent attitudes may help to ensure an effective presentation of fertility preservation options.

Of the various themes that surfaced among the focus groups in our study, none was more frequently discussed by both survivors and their parents than that of hindsight regret. From the survivors' perspective, this involved a retrospective realization of the importance of fertility preservation, coupled with regret that the issue had not been addressed at the time of cancer diagnosis. Parents expressed similar regrets, as well as a strong sense of personal guilt that they themselves had not brought up fertility concerns on their child's behalf. Both groups wished in hindsight that their physicians would have brought up the issue of fertility preservation and discussed it with them. Considering the aforementioned tendency of providers to table fertility discussions when confronted with perceived parental or patient discomfort or disinterest, these views highlight the potential repercussions of such deferrals, as reluctance to proceed with fertility discussions may lead to regret and guilt later on in life for all involved parties.

The recurrently expressed desire for fertility specialist involvement aligns with contemporary initiatives that advocate increased movement towards interdisciplinary collaboration in provider efforts to address cancer patients' reproductive concerns. Studies regarding the implementation of fertility preservation in clinical practice have regularly espoused a multidisciplinary approach to care; such an approach draws upon the combined expertise of both oncologic and reproductive specialists to tackle the decision-making intricacies found at the intersection of fertility risk assessment and cancer treatment planning.^{20,21} These collaborative efforts may lead to the development of experience-based decision algorithms and comprehensive care strategies to assist patients and providers in navigating these complex issues.^{21,22}

In assessing the attitudes of survivors and parents based on their personal experiences toward the inclusion of pediatric and adolescent patients in fertility preservation discussions, survivors' responses were mixed as to whether it would have been beneficial for them to be directly involved in the discussion or if having their parents represent them would have been more appropriate. Many survivors focused on their young age and how that hindered them from being able to recognize the issue of fertility and fully grasp the complexities of the discussion at the time. Interestingly, survivors placed a greater thematic emphasis on the notion of being too young for fertility discussions than their parents did, as most parents retrospectively felt that their children should have been involved in discussions, regardless of their age at the time of diagnosis. These viewpoints bear careful

consideration, particularly in light of practitioners' propensity to direct fertility discussions towards parents rather than the pediatric patients themselves.¹⁵

The findings of our study also call into question the validity of the provider perception that parents are embarrassed or made uncomfortable by fertility preservation discussions. The parents in our focus groups who were involved in fertility discussions rarely recounted any feeling of embarrassment or discomfort incurred from the discussion of their children's fertility prospects or the concept of sperm banking. In contrast, parents more frequently commented that fertility discussions provided a sense of hope, with the implied expectation that their children might survive long enough for future fertility to be of concern. Rather than embarrassment, parents felt the discussions fostered a sentiment of optimism and encouragement in the midst of a difficult experience. These viewpoints are consistent with accounts from other qualitative studies of pediatric fertility preservation counseling, which have reported that discussion of fertility preservation can often be interpreted as a message of hope for both patients and their families alike.¹⁵

In a 2008 study, Ginsberg et al. also undertook a qualitative investigation of the attitudes of adolescent and young adult oncology patients and their parents towards sperm cryopreservation. Their approach employed questionnaires administered to 50 patients who had been offered sperm banking, as well as their parents.²³ Notably, only four of the patients, and none of the parents, reported a definitively negative initial response towards the option to bank sperm, with one of those four opting for cryopreservation in the end. Patients and parents agreed that early discussion (within one week of cancer diagnosis) was optimal to prevent any delay of cancer treatment, although approximately 20% had to delay treatment in order to bank sperm and felt that the significance of fertility preservation was enough to merit this delay. Interestingly, given the aforementioned provider perception of patient and parent discomfort in fertility preservation discussions, Ginsberg et al. elicited mean "comfort ratings" (on a 1 to 5 scale, with 5 being *completely comfortable*) of 3.34 from the patients and 3.78 from their parents. This corroborates our study's finding that patient and parent discomfort levels are often overestimated by providers. Ultimately, respondents unanimously indicated that attempting to bank sperm was the right decision for them, including patients who were unsuccessful in their attempts.²³

There are several limitations inherent to our study. The potential for recall bias on the participants' part is a theoretical vulnerability intrinsic to retrospective studies of this nature. Also notable is our relatively small sample size drawn from a single institution. Additionally, the nature of our cohort (being already enrolled in an institutional cancer registry with a demonstrated willingness to be contacted for the study) points to a more proactive population that may be inclined to place greater emphasis on post-therapy fertility. A larger, more diverse cohort from across multiple institutions would likely represent a broader range of cultural and socioeconomic backgrounds, thus introducing greater heterogeneity of expressed viewpoints. These supplemental perspectives would be worthwhile to explore in any future follow-up studies. In looking forward, it is our intention that knowledge of the themes garnered from this qualitative

investigation will pave the way for future, more quantitative approaches to fertility preservation research within this unique patient population.

Conclusion

Our study highlights a noteworthy discrepancy between oncologists' pervasively-held preconceptions of pediatric patients' and their families' attitudes towards fertility preservation and the authentic attitudes expressed by adult-aged male survivors of pediatric cancer and their parents. While the importance of fertility preservation was generally not instinctively recognized by survivors or parents at the time of cancer diagnosis, retrospective consideration revealed that the issue of fertility frequently emerged as a significant concern later in life. Survivors and their parents consistently regretted that the issue of fertility preservation was not raised by the treating physician, as they held their providers chiefly responsible for initiating fertility preservation discussions and serving as their primary source of information. Many participants also wished that a fertility specialist had been consulted and involved in the process. Lastly, nearly all participants called for the active inclusion of pediatric patients in the fertility preservation discussion and decision-making process.

Although formal recommendations have been issued encouraging oncologists to discuss fertility preservation with patients and families as early as possible following oncologic diagnosis, lack of awareness and incomplete adoption of these recommendations within the medical community continue to impede fertility preservation efforts. Looking forward, our study findings may be practically applied towards the development of educational materials for physicians and medical teams to facilitate fertility preservation discussions between providers, patients, and their families. Through such endeavors, a greater understanding of the thematic perspectives elicited from the pediatric cancer survivors and parents in this study may foster future efforts to correct provider misconceptions and reduce barriers to addressing fertility preservation in this patient population.

Disclaimer

The findings of this study were presented at the American Psychosocial Oncology Society's 9th Annual Conference, February 23–25, 2012, in Miami, FL, as well as the American Urological Association's 107th Annual Conference, May 19–23, 2012, in Atlanta, GA.

Author Disclosure Statement

No competing financial interests exist.

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