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FERTILITY PRESERVATION

Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancer

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Abstract
Purpose Diminished reproductive capacity is a devastating consequence of life-sparing therapies for childhood malignancy. In 2006, the American Society of Clinical Oncology (ASCO) published fertility preservation recommendations (ASCOR) emphasizing the importance of early discussion and intervention for fertility preservation strategies. Using the Survey for Preservation of Adolescent REproduction (SPARE), we sought to determine fertility preservation attitudes and practice patterns post-ASCOR from pediatric oncology specialists nationwide.
Materials and methods The SPARE survey consists of 22 questions assessing pediatric oncology specialists' attitudes and practice patterns toward fertility preservation. Broad perspectives on fertility preservation, including a willingness to discuss fertility, knowledge of current fertility preservation methods and awareness of ASCOR, were assessed.

Capsule The SPARE survey captured marked disparities between pediatric oncologists' attitudes and practice patterns regarding fertility preservation for male and female pediatric oncology patients.

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Results The majority of respondents acknowledged that fertility threats are a major concern for them and agreed that all pubertal cancer patients should be offered a fertility consultation, but only 46% reported they refer male pubertal cancer patients to a fertility specialist prior to cancer treatment >50% of the time, and only 12% reported they refer female pubertal cancer patients to a fertility specialist prior to cancer treatment > 50% of the time. While 44% of respondents were familiar with the 2006 ASCOR, only 39% of those utilized them to guide decision-making in greater than half of their patients.
Conclusion Our study demonstrates pediatric oncologists' motivation to preserve fertility in pediatric cancer patients; however, barriers to both gamete cryopreservation and referral to fertility specialists persist. Female pubertal patients are referred to fertility preservation specialists with much less frequency than are male pubertal patients, highlighting a disparity.

Keywords Pediatric oncology · Cryopreservation · Fertility preservation · Cancer · Survey

Introduction

In an era of improving treatment and survival of pediatric oncology patients, fertility preservation has become a central survivorship issue. Prior to new advances in the field of reproductive medicine and fertility preservation, many clinicians believed that the process of gamete cryopreservation was a futile endeavor. For instance, early studies suggested that men with testicular carcinoma were significantly less likely to be candidates for pre-chemotherapeutic or pre-radiation sperm cryopreservation than were healthy young men. The authors of these studies contended that sperm cryopreservation was an unrealistic solution for future infertility as stored sperm samples were generally not adequate to facilitate attempts at intrauterine insemination [1, 2]. This paradigm became outdated with the development of intracytoplasmic sperm injection (ICSI) in 1992. ICSI is a method used in conjunction with in vitro fertilization (IVF) whereby an individual spermatozoon is directly injected into an aspirated mature oocyte. Thus, fertilization and subsequent pregnancy can often be achieved in the setting of severely impaired fertility, such as markedly reduced sperm concentration or ovarian failure. As a result, ICSI has dramatically expanded the opportunities to overcome both severe male and female factor infertility.

Following the development of ICSI, a discrepancy between available fertility preservation techniques and their use emerged. This trend was identified in a study published in 1999 in which ASCO members in Minnesota were surveyed regarding fertility preservation. Forty-six (28%) of the 165 members responded. Only 26% of those responding were familiar with ICSI, and the respondents estimated that only 27% of their patients chose to cryopreserve sperm [3]. In 2000, other investigators performed a large cross-sectional survey of 110 centers that were part of POG (Pediatric Oncology Group) to establish the current level of best clinical practice for sperm and ova, as well as pre-pubertal tissue collection and storage [4]. The study revealed an absence of clinical guidelines at all institutions, and a lack of agreement between institutions with regard to indications or methodology for gamete preservation. Ninety-three percent of the responding centers reported offering sperm cryopreservation and only 10% reported offering ova cryopreservation. Fifteen percent of the centers reported offering sperm cryopreservation to males prior to completion of sexual development, and 3% offered oocyte cryopreservation to females prior to sexual maturation. Several studies have since demonstrated suboptimal fertility preservation counseling and underutilization of fertility preservation techniques [5, 6].

In 2005, the American Society for Reproductive Medicine (ASRM) published manuscripts identifying fertility preservation for cancer patients as an important topic [7, 8]. This was followed in 2006 by the American Society of Clinical Oncologists (ASCO) which published fertility preservation recommendations (ASCOR) to the oncology community [9]. Tenets of the document included the recommendation to discuss fertility preservation options with patients shortly after cancer diagnosis, preferably before initiation of treatment, and to refer them to a fertility specialist with expertise in fertility preservation methods. If eligible, men should seek sperm cryopreservation, and in cases of azoospermia or anejaculation, consider alternative methods of sperm collection [9]. Similarly, women could pursue embryo cryopreservation, conservative gynecological surgery, or oophoropexy. Investigational fertility preservation techniques such as cryopreservation of ovarian tissue, cryopreservation of oocytes, and ovarian suppression were also discussed.

Since release of the ASCOR, only a few studies have been published regarding fertility preservation utilization among pediatric oncology patients [10–14]. Despite the existence of the ASCO recommendations, similar themes emerge from these studies, including a need for improved communication between pediatric oncology providers and specialists in reproductive medicine, a lack of fertility preservation counseling by health care providers, patient and patient guardian misconceptions, and poor patient guardian fertility preservation satisfaction rates [15–17]. In fact, one study showed only 29 of 97 (30%) parents were satisfied with the fertility preservation counseling they received with regard to their child [18].

The relevance of the discrepancy between practice patterns and available fertility preservation techniques becomes readily apparent when considering the high incidence of fertility-threatening cancers and the deleterious effects of subsequent treatment on reproductive health [19]. Approximately 12,400 adolescents and children under the age of 20 are diagnosed with cancer each year in the United States, and over 20,000 pediatric or reproductive aged patients are treated with chemotherapy and/or radiation annually [20]. Even prior to initiation of any therapy, the disease processes of the cancer itself can threaten fertility through inflammatory or immunity-related pathways [21]. Direct deleterious effects on fertility from pediatric malignancies have been widely documented in testicular cancer and Hodgkin lymphoma [9].

Improved patient survival with the newest pediatric cancer treatment protocols belies the increased rates of gonadotoxicity from chemotherapy, radiation, and debulking surgery. Risks of such treatments in males include disruption of the hypothalamic-pituitary-gonadal axis, cytotoxic effects on the testicular germinal epithelium, impairment of penile erectile function, sympathetic nervous system damage that subsequently prevents normal seminal emission and ejaculation, and injury to the genital duct system, the conduit for normal sperm transport. The testis is one of the most radiosensitive organs in the body, with radiation therapy causing germ cell loss in a dose-dependent fashion and even very low doses affecting spermatogonia [22]. Similarly, chemotherapy and radiation in female cancer patients can result in premature menopause and ovarian dysfunction secondary to ovarian toxicity. The risk of gonadotoxicity is related to the patient's age at the time of treatment, pre-existing gonad function, and the dose and duration of treatment [23]. In addition, the mechanism of action of agents determines their impact on gonad function. For example, drugs directed towards resting or dormant follicles may induce premature menopause whereas cell cycle arresting agents will impact the cohort of growing follicles and may result in temporary ovarian insufficiency [24]. Alkylating agents in particular have been shown to be one of the most toxic classes of chemotherapeutic medications available and are associated with a high risk of post treatment infertility in both females and males.

Due in large part to the high efficacy of today's cancer treatments, the 5-year survival rate for patients under the age of 15 with cancer at any site is approaching 75% [25]. From 2000 to 2004, 12% of patients with Hodgkin lymphoma were diagnosed under the age of 20, and the cancer carried an 85% 5-year survival rate for patients in this age group [26, 27]. Similarly, approximately 5.5% of testicular cancers were found in pediatric patients, and carried a 95.4% survival rate [26, 27]. With a greater number of pediatric oncology patients surviving their disease, the impact of cancer and cancer therapies on future reproductive health has become a crucial issue for these patients and patient guardians. In this study, we sought to obtain robust, post-ASCOR data from pediatric oncology specialists regarding their attitudes towards fertility preservation and their practice patterns regarding their male and female patients. Our objective was to assess whether the gap between fertility preservation options and practice patterns has narrowed with the advent of ASCOR.

Methods

In order to assess post-ASCOR practice patterns and attitudes of pediatric oncology specialists, our group created the Survey for Preservation of Adolescent REproduction (SPARE). This was an institutional review board approved study which consisted of 22 question groups (with 61 total question items) assessing various domains of fertility preservation attitudes and practice patterns for both prepubertal (1–12 years of age) and pubertal (13–18 years of age) cancer patients, stratified for males and females. The survey asked respondents about their knowledge of specific fertility preservation methods, their familiarity with ASCOR, and their practice patterns with regard to fertility preservation (Questions 1–16). The survey also assessed the demographics of survey participants (Questions 17–22). The survey was constructed and administered through SurveyMonkey™, a secure, online survey-hosting site.

A survey announcement with an accompanying internet link to the survey site (at www.surveymonkey.com) was emailed to all members of a nationwide pediatric oncology subspecialty group via the group's list serv. We paid a service fee to the group, and they distributed the email to their membership via the list serv. We did not have direct access to the email list serv, as is the policy of the group to protect members' privacy. A follow-up email regarding the survey was subsequently sent to all members on the list serv approximately four weeks later; the email message encouraged recipients to complete the survey if they had not yet done so. Finally, two members of our team called the offices of pediatric oncologists throughout the country (identified via state-by-state internet search) after the second email. These team members left messages with phone staff encouraging the pediatric oncologists in the respective practices to complete the emailed survey if they had not yet done so. Again, we were blinded and remain blinded to the list of individuals who did and did not participate in the survey.

In total, 1428 individuals were contacted via email and invited to complete the survey. All data were analyzed using Survey Monkey's™ Program Statistics and Microsoft Excel software. No data were collected from non-responders.

Results

Respondent demographics and response rate

Of the 1428 individuals contacted by email, 209 (15%) initiated the survey. Some respondents skipped particular questions in the Fertility Preservation Knowledge, Attitudes and Practice Patterns portion of the survey (Questions 1−16) and/or questions in the Demographics portion of the survey (Questions 17−22). When compared to individuals starting the survey (n=209), the number of individuals responding to specific questions in the 1−16 Question group ranged from 180/209 (86%) to 209/209 (100%). A total of 170/209 (81%) answered all 22 survey questions (Fertility Preservation Knowledge, Attitudes and Practice Patterns portion [Questions 1−16] plus the Demographics portion [Questions 17−22] of the survey).

Responses to specific questions were used in the data analysis if they were provided, and the respondents were not counted in the denominator for a particular question if they did not provide an answer for that question. Given the anonymous nature of the survey, it is impossible to accurately characterize the group of individuals who did not respond to the survey.

The respondent demographics are reported in Table 1. The majority of survey respondents were pediatric oncologists (>92%), although some pediatric oncology fellows and nurse practitioners also participated. Respondents were primarily affiliated with a university practice (79%), had an average age of 45 years, and 53% were male. Respondents saw approximately 30 total adolescent male and female patients (age 18 and under) for initiation of cancer therapy per year. The three most commonly treated cancers in order of decreasing frequency were leukemia/lymphoma, brain malignancy, and osteosarcoma.

All results presented below are shown as percentages of the total number of responses for the particular survey item in question.

Table 1 Respondent demographics

Total number of respondents who started survey	209
Total number of respondents who completed survey	180 (86%)
Gender of Respondents (n=180)	
Male	96 (53%)
Female	84 (47%)
Age of Respondents (n=178)	
Average age 45 years of age	
Age range 30 to 67 years of age	
30−39 years of age	53
40−49 years of age	71
50−59 years of age	42
>60 years of age	12
Type of Practitioner (n=180)	
Pediatric oncologist	167 (93%)
Nurse or nurse practioner	5 (3%)
Reproductive endocrinologist	2 (1%)
Other or no answer	6 (3%)
Type of Practice (n=173)	
University practice	137 (79%)
Private practice- urban	29 (17%)
Private practice- suburban	6 (4%)
Private practice- rural	1 (1%)
Most Common Cancer Diagnoses of Patients (n=170)	
1. Leukemia and lymphoma	140 (82%)
2. CNS tumors	10 (6%)
3. Osteosarcoma	7 (4%)
4. Other sarcomas	6 (4%)
5. Other	7 (4%)

Knowledge of fertility preservation

While 74% of respondents reported awareness of ovarian tisuse cryopreservation, a minority of respondents (36%) were familiar with emergency IVF and just over half (55%) knew about ICSI. Furthermore, only 44% of respondents were familiar with the 2006 ASCOR.

General fertility preservation attitudes and practice patterns

According to the survey, a majority of respondents agreed or strongly agreed that fertility threats to their patients are of major concern to them as physicians (81%) and to their patients' parents (84%). In fact, 85% reported that both patients and their parents have asked about potential fertility threats associated with cancer treatment. Ninety-nine percent of respondents felt that all pubertal patients should be told about the potential impact of drug and radiation therapy on reproductive health prior to treatment; 79% believed that pubertal patients should be referred to a fertility preservation specialist prior to treatment. While 93% of respondents felt that all prepubertal patients should be told about potential drug or radiation damage prior to treatment, only 36% thought that all prepubertal patients should be referred to a fertility preservation specialist before treatment. Finally, more respondents believed that pubertal patients should be offered tissue cryopreservation, either testicular or ovarian, than prepubertal patients. Additional results of oncologists' fertility preservation attitudes regarding male patients (Table 2) and female patients (Table 3) are presented.

Table 2 Fertility preservation attitudes: male cancer patients

Survey Question	Percentage Agree/ Strongly Agree (%)
All pubertal male patients (13–18 years of age) should be told about potential drug or radiation damage to the testicles prior to treatment.	100
All prepubertal male cancer patients (1–12 years of age) and their parents should be told about potential drug or radiation damage to the testicles prior to treatment.	93
Success rates of infertility treatment with cryopreserved sperm are high enough to justify sperm banking.	89
Male cancer patients and their parents have asked about potential fertility threats associated with cancer treatment.	82
Fertility threats to my male patients are a major concern for their parents.	81
Fertility threats to my male patients are a major concern for me.	80
The expense of sperm banking and storage is worthwhile.	75
Sperm banking and storage is affordable.	36

Fertility preservation attitudes and practices: male cancer patients

While 86% of respondents agreed that all pubertal males should be referred to a fertility preservation specialist prior to cancer therapy, only 66% do this (≥50% of the time) (Fig. 1a). Ninety-two percent agreed that all pubertal males should be offered sperm banking prior to treatment, and 85% report doing this (≥50% of the time) (Fig. 1b). In cases where the male has azoospermia or is unable to provide an ejaculated sample, 23% agreed that testicular tissue cryopreservation should be offered, but only 10% do this (≥50% of the time) (Fig. 1c). While 73% of respondents agreed that all pubertal males should be referred to a fertility preservation specialist post cancer therapy, only 50% do this (≥50% of the time) (Fig. 1d). Finally, respondents were asked to consider their prepubertal male patients with cancer. Fifteen percent of respondents agreed that all prepubertal males should be offered testicular tissue cryopreservation prior to cancer treatment, but only 5% offer this (≥50% of the time) (Fig. 1e).

Fertility preservation attitudes and practices: female cancer patients

While 73% of respondents agreed that all pubertal females should be referred to a fertility preservation specialist prior to cancer therapy, only 23% do this (≥50% of the time) (Fig. 2a). Forty-six percent agreed that all pubertal females should be offered ovarian tissue cryopreservation prior to treatment, but only 13% reported doing this (≥50% of the time) (Fig. 2b). While 77% of respondents agreed that all pubertal females should be referred to a fertility preservation specialist post cancer therapy, only 46% do this (≥50% of the time) (Fig. 2c). Finally, respondents were asked to consider their prepuberal female patients with cancer. Twenty-four percent of respondents agreed that all prepubertal females should be offered ovarian tissue cryopreservation prior to cancer treatment, but only 6% offer this (≥50% of the time) (Fig. 2d).

Sperm banking

When asked about the youngest age at which they would offer sperm banking, 121 out of the 170 respondents provided a numerical answer, with a mean age of 12.6 years and a median age of 13 years. The remaining respondents indicated that they offered banking based on pubertal status, Tanner staging, or ability to ejaculate. Eighty-five percent of respondents reported offering sperm banking within 1 week of cancer diagnosis. In the event of the patient's death, 46% said that they recommend that the banked sperm be thawed and destroyed, 37% recommend it be given to the patient's parents, and 23% recommend donating the sperm to a research facility.

Barriers to sperm banking

Of the choices provided on the survey, the most likely reasons for a physician to not recommend sperm banking was a patient having a poor survival prognosis, an aggressive disease requiring the immediate initiation of

Table 3 Fertility preservation attitudes: female cancer patients

Survey Question	Percentage Agree/ Strongly Agree (%)
All pubertal female patients (13–18 years of age) should be told about potential drug or radiation damage to the ovaries prior to treatment.	99
All pre-pubertal female cancer patients (1–12 years of age) and their parents should be told about potential drug or radiation damage to the ovaries prior to treatment.	94
Female cancer patients and their parents have asked about potential fertility threats associated with cancer treatment.	88
Fertility threats to my female patients are a major concern for their parents.	87
Fertility threats to my female patients are a major concern for me.	83
I am aware of research on fertility preservation for young women with cancer.	75

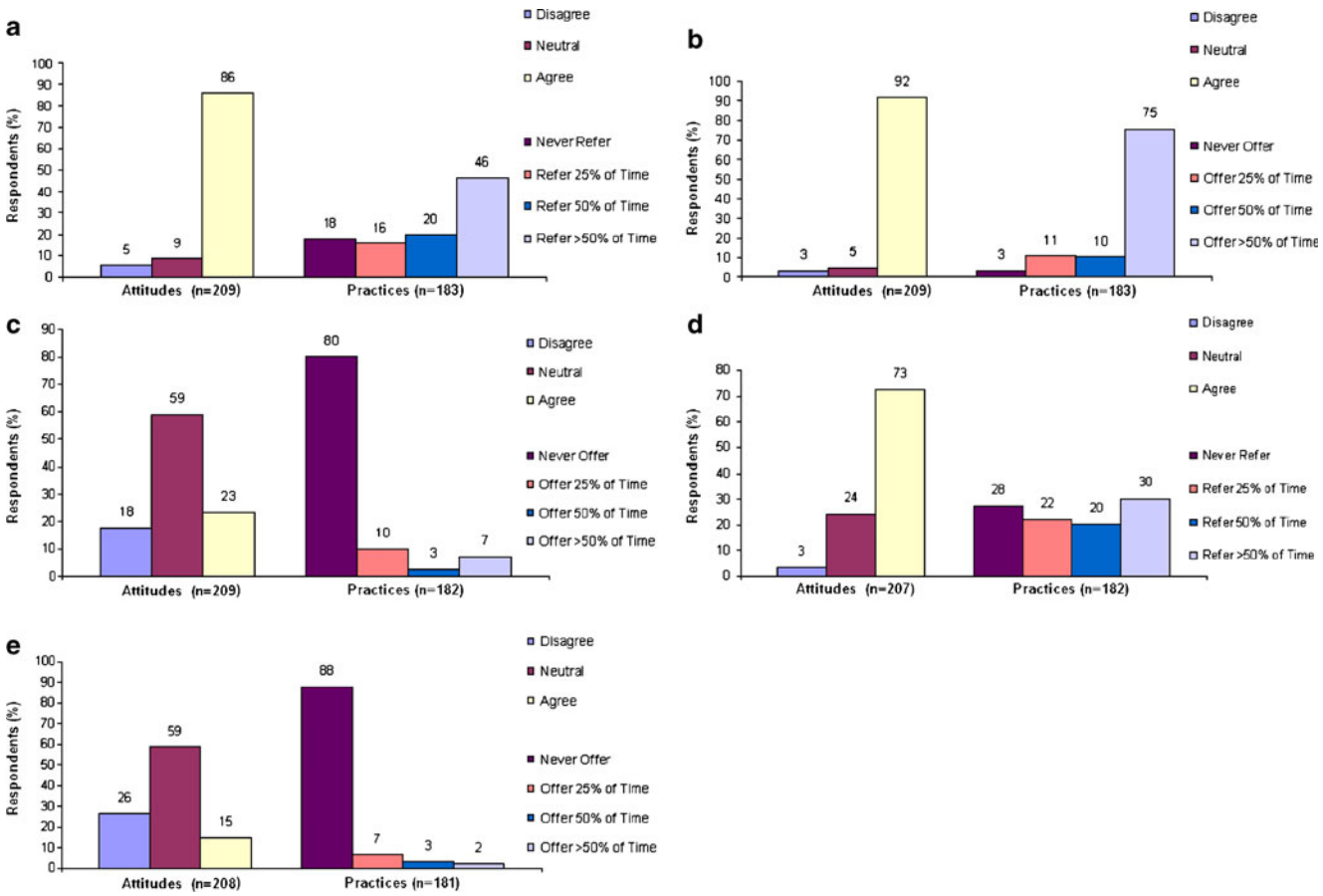

Fig. 1 **a**–**e** Attitudes vs. practices: male cancer patients (pubertal and pre-pubertal). **a** All pubertal males should be/are referred to FP specialist pre-cancer treatment; **b** All pubertal males should be/are offered sperm banking pre-cancer treatment; **c** All pubertal males should be/are offered testicular tissue cryopreservation in cases of azoospermia or inability to ejaculate; **d** All pubertal males should be/are referred to FP specialist post-cancer treatment; **e** all pre-pubertal males should be/are offered testicular tissue cryopreservation

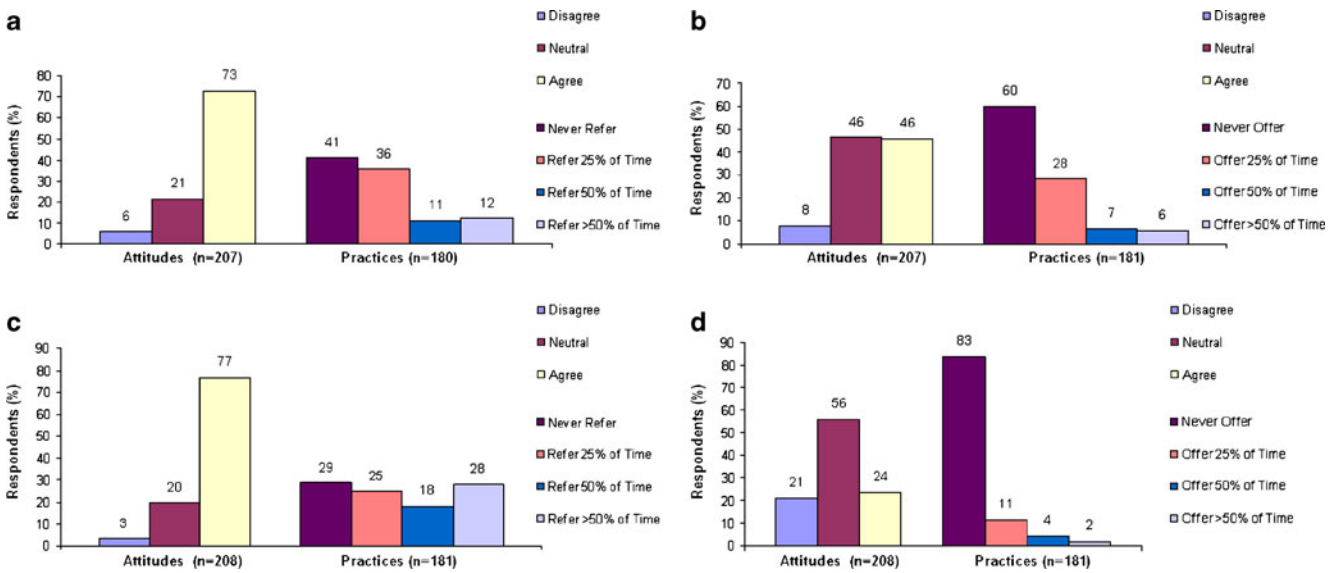

Fig. 2 **a**–**d** Attitudes vs. practices: female cancer patients (pubertal and pre-pubertal). **a** All pubertal females should be/are referred to FP specialist pre-cancer treatment; **b** All pubertal females should be/are offered OTC pre-cancer treatment; **c** All pubertal females should be/are referred to FP specialist post-cancer treatment; **d** All pre-pubertal females should be/are offered OTC pre-cancer treatment

treatment, and the patient's parents not providing consent. Discomfort with discussing sperm banking with their pubertal patients was identified as the least likely reason for physicians to not recommend sperm banking.

Similarly, respondents indicated that the most common reasons pubertal male patients or their parents refused sperm banking prior to treatment were the desire to initiate treatment as soon as possible, not wanting to be concerned with possible infertility, and the patients (or their parents) not being concerned with parenthood at the time of treatment. Of the choices given, wanting to conceive with fresh semen and believing that sperm banking is not worthwhile were identified as the least likely reasons for patients and their parents to refuse banking.

Finally, respondents were asked to estimate the total dollar cost (freezing plus storage) for the first year of cryopreserving sperm. Responses ranged from $100 to $500,000, with mean and median values of $4547 and $500, respectively. Thirteen percent (21/166) of the respondents did not provide an estimate.

Discussion

The 2006 ASCOR were developed with the purpose of providing information to health care providers about available fertility preservation methods and related issues in cancer patients. In this study, we sought to obtain post-ASCOR fertility preservation data from pediatric oncology specialists nationwide, and to ascertain to what degree these recommendations have been incorporated into their practices. Our results revealed that a disconcerting majority of respondents reported not being familiar with the 2006 ASCOR. Furthermore, over 60% of respondents reported utilizing the 2006 ASCOR in healthcare decision-making only a quarter of the time or less.

With our study's demonstatration of lack of awareness and implementation of the 2006 ASCOR, it is not surprising that disparities between many of the fertility preservation attitudes and practice patterns of the surveyed pediatric oncologists were very similar to those reported prior to the publication of these recommendations (Figs. 1 and 2). Regarding males with cancer, comparable data were reported in 2002 in a study of oncologists that showed 91% of respondents agreed that sperm banking should be offered to all men at risk of impaired fertility due to cancer treatment. However, 48% either never brought up the topic or mentioned it to less than a quarter of their eligible male patients [5]. This discrepancy between attitudes and practices is further highlighted in response to pubertal female patients (Fig. 2). The gender disparity in fertility sparing options means that survivors of cancer will have different expectations for a quality adult life because of fertility threats that were not addressed at the time of diagnosis.

Fertility preservation options for pre-pubertal cancer patients

In reference to pre-pubertal cancer patients, respondents' attitudes were congruent with their practices. For example, only 15% agreed that pre-pubertal males should be offered testicular tissue cryopreservation and 24% agreed that pre-pubertal females should be offered ovarian tissue cryopreservation prior to cancer treatment. Correspondingly, 88% and 83% never offer tissue cryopreservation to their male and female pre-pubertal patients, respectively (Fig. 1e and 2d). Clearly, no disparity exists between attitudes and practices towards pre-pubertal cancer patients. Given the limitations of biology at this time, the investigational cryopreservation of immature gonadal tissue from pre-pubertal patients is one potential fertility preserving option for pre-pubertal cancer patients. It is unclear if and how scientific advances will facilitate the successful use of this tissue for reproductive purposes in the future.

Barriers to treatment and referral

One possible explanation for the lack of utilization of the ASCOR is simply a lack of knowledge of current fertilization preservation techniques. Our study showed a lack of familiarity with fertility preservation, as well as some of the most important infertility treatments, including ICSI and emergency IVF. Awareness of established fertility preservation techniques and assisted reproductive technologies is essential to ensure appropriate counseling and referral of young cancer patients who may wish to pursue the option of biological parenthood in the future. The SPARE study provides an excellent platform to re-emphasize to all pediatric oncology specialists that viable options for fertility preservation for oncology patients exist and others, while investigational, may potentially hold promise for even the youngest patients (e.g., testicular and ovarian tissue cryopreservation).

An additional barrier to pursuing fertility preservation is the lack of adequate time prior to the start of cancer treatment for some patients. This is particularly true for pubertal female cancer patients. Emergency IVF and oocyte cryopreservation each require up to 2–3 weeks for menstrual cycle synchronization, ovarian stimulation, and oocyte retrieval. For patients with strict time constraints, alternative options should be discussed. The severity of the malignancy and the risk of rapid progression may dictate the immediate initiation of treatment; thus, oncologists may not discuss these fertility preservation options with their patients. Furthermore, the costs of assisted reproductive

technologies may be prohibitive to some patients, and physicians may not be aware of resources available to assist with these expenses.

Pediatric oncology patients present a unique set of complexities, as they are undergoing life-saving therapies yet may be too young to fully comprehend the reproductive-threatening consequences of those therapies. Parents are often making decisions for their children with little to no input from them [10, 28]. Ethical and legal considerations are also at play, as adolescent patients are minors who cannot give informed consent unless emancipated from their parents or guardians [29]. In all but exceptionally rare circumstances, parental consent must be obtained prior to the performance of any fertility preservation option. Some young adults may have a clear understanding of the issues and wish to voice their reproductive choice. At times, these choices may contradict their parents' wishes and pose a real dilemma for families. Thus, a delicate balance must be brokered which requires a patient, informed, and skillful healthcare provider, as well as adequate time. This is often a challenge given the urgent need for treatment in many patients.

In males, no reliable prepubertal fertility preservation techniques of spermatogonia A stem cells exist. Spermarche, the ability of the spermatogonia A stem cells to develop into mature spermatozoa, has typically occurred by the time most boys experience their first nocturnal emission. Spermarche occurs in boys by around age 12 years, but age range varies. Referral of prespermarche boys to a fertility preservation specialist may help with counseling, but no effective preservation methodology has yet been established [21]. Investigational techniques, such as testicular tissue harvesting for autotransplantation, and testicular tissue extraction for transplantation into immunodeficient mice are currently being explored.

Options for fertility preservation in prepubertal girls have also been challenged by biologic, psychosocial and ethical limitations [19]. Prior to the developmental of recent investigational techniques, the mainstay of fertility-sparing options was to utilize methods that aimed to reduce the risk of gonadotoxic effects. For example, chemotherapeutic agents and doses known to be less toxic can be selected to decrease the impact on the ovaries without compromising the clinical outcome of patients. Fractionating the dose of total body radiation and employing the use of ovarian shields during radiotherapy also help reduce risk. For young girls receiving pelvic radiation, oophoropexy can be performed. Through this outpatient surgical procedure, the ovaries are suspended above the pelvis and removed from the field of radiation. The risk of ovarian damage is reduced, although not entirely eliminated, as there can be extension of the radiation beyond the pelvis [30]. The use of GnRH agonists to downregulate the HPG axis prior to and during chemotherapy remains controversial, as conflicting results regarding their true protective effects have been reported [31, 32].

Most centers do not consider girls under the age of 18 to be candidates for assisted reproductive technologies such as embryo cryopreservation, primarily due to concerns surrounding informed consent, use of donor sperm and the delay in cancer treatment while patients pursue these options. Thus, the need for alternative fertility sparing options is truly highlighted in this patient population.

Fundamentally, fertility preservation for men and women revolves around the common themes of gamete storage and later utilization. However, the currently available reproductive options for female survivors, as compared with their male counterparts, offer a very different prospect for future fertility. Whereas men possess the proven success of sperm cryopreservation with subsequent use in IVF/ICSI, female survivors have few established options. Options traditionally available to women, such as ovarian transposition, embryo cryopreservation, and mature oocyte cryopreservation present unique limitations when applied to cancer patients, particularly those of childhood age. The promise for some female survivors may lie in the strides made in experimental protocols, such as ovarian transplantation and in vitro follicle maturation [31].

Study limitations

Our study presents data from 209 participants, outnumbering participation in the majority of similar studies (pre- or post-ASCOR) [3, 5, 6, 10–14]. Nonetheless, it is important to note that the response rate to this survey was low. Of the 1428 individuals contacted regarding the survey, only 209 (15%) individuals started the survey. Of these 209, 170 (81%) provided answers to every question and 39 (19%) skipped one or more questions. In addition to the low response rate, this survey may suffer from a very strong participation bias, with respondents being more interested in fertility preservation than nonrespondents.

The SPARE study is also somewhat unique in comparison to previous studies in that we sought a diverse, nationwide response, and thus the data are not subject to potential inherent biases related to geographic regions. Our response rate of 15% was likely the result of the survey's length, lack of completion incentives, and the general frequency with which email surveys are sent to health care providers. The discrepency between number of surveys started (209) and the number completing every question (170) is most likely explained by the fact that the online survey was divided into 3 pages, but could be incorrectly interpreted as finished after only the first of three pages was completed. As such, the second and third pages had slightly fewer responses. The final portion of the survey (Questions

17–22) requested limited demographic information, and some respondents may have skipped these questions in an effort to help maintain their own anonymity. In addition, despite the survey being anonymous, some degree of voluntary reporting bias likely occurred. Physicians with an interest in fertility preservation practices may have been more familiar with ASCOR, and more likely to respond to the survey. The majority of respondants were affiliated with universities (79%) versus private pediatric oncology practices (21%). It is possible that physicians associated with a university practice are more exposed to issues of fertility preservation and may have more resources available to them. If voluntary reporting bias did occur, our data likely overestimate the true pediatric fertility specialist knowledge and fertility preservation practice rate.

Conclusions

With the advent of improved cancer treatments and the subsequent rise in survival, a host of new health care and quality-of-life issues has emerged for young cancer patients. While advances in surgery, radiation, and chemotherapy have improved survival rates, these therapeutic agents may also permanently impact the reproductive capacity of cancer survivors, including adolescents. Through knowledge of current fertility preservation techniques available and use of the ASCOR, health care providers can optimize the reproductive health of young cancer patients.

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