Published in final edited form as:

Pediatr Hematol Oncol. 2009 June ; 26(4): 252–260. doi:10.1080/08880010902901294.

Sperm Cryopreservation Practices Among Adolescent Cancer Patients At Risk For Infertility

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Abstract

To assess sperm cryopreservation among males newly diagnosed with cancer aged 13 years and older, attending oncologists assigned infertility risk (yes/no) to patients and reported whether their patients engaged in sperm cryopreservation. Only 28.1% of informed at-risk patients banked sperm. Utilization of sperm banking was significantly associated with a diagnosis of CNS malignancy or non-CNS solid tumor diagnosis, higher socioeconomic status, and not being a member of an Evangelical religious group. These results suggest that sperm banking is underutilized among adolescent males newly diagnosed with cancer, and that strategies to increase the engagement in this fertility preservation method are needed.

Keywords

sperm cryopreservation; fertility; assisted reproduction; childhood cancer

Introduction

Despite the known adverse effects of specific cancer treatments on fertility, only between 18–24% of young men at high risk for treatment-related infertility cryopreserve sperm prior to cancer treatment [1,2,3]. These already less than optimal rates of sperm banking may be even lower among young minority males and in those of low socioeconomic status (SES) [4]. It is not clear why sperm banking is underutilized, particularly in light of the high priority that survivors of childhood cancer place on fertility [5] and the high psychological distress associated with fertility loss. Several studies have suggested that factors such as lack of and/or inaccurate knowledge of infertility risk at the time of diagnosis contribute to the low frequency of sperm cryopreservation in this cancer group [1,6]. In addition, reports from centers in the United Kingdom, where the cost of sperm banking is covered under the national health care system, suggest that the youngest teens have more difficulty producing semen samples and are more anxious about going to clinic in order to engage in sperm banking procedures [7].

The purpose of this preliminary study was to assess the proportion of newly diagnosed adolescent and young adult male patients at risk for compromised fertility based on cancer treatment, to evaluate rates of physician-patient communication regarding treatment-related

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Declaration of Interest

None of the authors have any financial or personal relationships which could influence the findings of this study.

infertility risk, and to describe sperm banking practices in this population. In addition, an important aim of this study was to assess demographic factors that may influence utilization of sperm banking. As older adolescents are more likely to be postpubertal and possibly more likely to be concerned with fertility preservation, we hypothesized that older age at diagnosis would be associated with increased sperm banking. We also predicted that adolescents from families with higher socioeconomic status and Caucasian adolescents would be more likely to engage in banking sperm.

Methods

All male patients aged 13 years and older who were newly diagnosed with cancer between July 1, 2006 and June 30, 2007 at St. Jude Children's Research Hospital were considered for this institutional review board-approved study. The oncologists caring for the identified patients were first asked to assign a yes/no response to the following question, "Was the patient at risk for infertility due to cancer treatment?" If the oncologist responded "no," then no further questions were asked. If the answer was "yes," then two follow-up questions were asked: "Was the risk of infertility discussed with the patient and/or family?", and "Did the patient bank sperm prior to the initiation of cancer treatment?" One hundred percent of the 14 oncologists approached for this study participated.

After identifying patients at risk for infertility, analyses were conducted to identify differences in demographic, medical, and cultural factors between those patients who did and did not bank sperm. Independent *t* tests were used for analyses of continuous variables, whereas Chi-square tests were used for analyses of categorical variables. Specific factors considered included: diagnosis (Central Nervous System (CNS) tumor, leukemia/lymphoma, or non-CNS solid tumor), age at diagnosis (in years), illness status (whether admitted to the hospital at or within 10 days of diagnosis), race/ethnicity (Caucasian, African-American, Latino, or multiracial), socioeconomic status (SES; high or low based on guidelines noted below), and religious affiliation (Catholic, Evangelical, other Christian, Jewish, or no religious endorsement). SES was determined using the Hollingshead index [8] to assign a score based on parent occupation. Insurance status (private or no insurance/public insurance) was taken into account in assigning SES scores, which were then recoded using a median split into high or low status groups. The religious affiliation of patients was categorized as Evangelical if they reported Evangelical, Baptist, or Pentecostal as their primary affiliation[9].

Results

A total of 66 patients with a mean age at diagnosis of 16.63 years (*SD* = 2.28, Range = 13.26 – 23.52 years) were eligible for this study. Of these 66 eligible patients, 34 (51.5%) were identified as at risk for infertility due to cancer treatment, based on oncologist report (mean age at diagnosis = 17.25, *SD* = 2.28, Range = 13.92 – 23.52 years). Physicians reported discussing infertility risk with 32 (94.1%) of the at-risk patients. One of the two patients who did not participate in fertility discussions had initiated treatment just prior to arriving at St. Jude, while the other was reported as being too sick at the time of diagnosis for banking to take place. Characteristics of the full sample and of the at-risk patients are shown in Table 1 as well as a side by side comparison of the patients who banked versus those who did not bank sperm. Only 9 (28.1%) of the 32 at-risk patients who participated in infertility risk discussions banked sperm. There was a trend indicating that older patients were more likely to bank sperm than younger patients (*t* (32) = 1.92, *p* = .06). Although sperm banking did not significantly differ by illness status (χ^2 = 2.63, *p* = .27), no patient who was hospitalized at the time of diagnosis (*n* = 4) banked sperm and only 2 of 9 patients who were hospitalized within 10 days of diagnosis banked. In regard to cancer diagnosis, those patients with CNS malignancy and non-CNS solid tumor were more likely to engage in sperm banking than were leukemia/lymphoma patients

($\chi^2 = 8.63, p < .02$). Utilization of sperm banking was also more likely among patients with higher socioeconomic status ($\chi^2 = 4.64, p < .05$).

With the small number of patients who banked sperm, banking did not differ by race/ethnic group. Similarly, when sperm banking practices were compared across the 5 religious categories, no differences were identified. Yet when religious groups were examined based on common attitudes towards sperm banking, some interesting findings were noted. Specifically, only one out of 18 patients with an Evangelical religious affiliation banked sperm. As a result, Evangelical participants were identified as being significantly less likely to bank sperm when compared to all other religions (including “none listed”), $\chi^2 = 8.60, p < .01$. The majority of Evangelical patients self-identified as Southern Baptists.

Discussion

Of the newly diagnosed adolescent patients informed of their risk for infertility by their pediatric oncologist, only 28.1% banked sperm. This rate was generally consistent with the findings of Schover et al. (1999) [3] in which retrospective reports of sperm banking practices among high risk young adult males surviving cancer were collected. This rate of sperm banking is disappointingly low, given reports that maintaining fertility is a high priority among cancer survivors and that infertility resulting from cancer treatment has been associated with psychosocial distress [10]. Although it could be argued that these low rates of sperm banking are due to the acute medical needs of those adolescents initially presenting to our institution (i.e. need to start treatment immediately and/or patients who presented as too ill for sperm banking), our data do not fully support this notion as utilization of sperm banking did not significantly differ by illness status. However, the finding that leukemia/lymphoma patients were less likely to bank sperm may reflect a lower likelihood of more acutely ill patients engaging in banking. As sperm banking should ideally take place prior to the initiation of cancer treatment, reduced levels of sperm banking among leukemia patients may, alternatively, be a function of the relatively reduced time between initial hospital presentation and the initiation of cancer treatment often experienced by this cancer group. Clearly, there are many factors that contribute to an adolescent's choice to bank sperm prior to cancer treatment. The current study enhances understanding of factors influencing this decision-making process by evaluating the impact of demographic, medical, religious and physician-patient communication issues in relation to sperm banking practices.

Regarding physician-patient communication, 94% of participating oncologists reported discussing fertility issues with those at risk for fertility problems based on their cancer treatment. This rate of discussion is much higher than others published in the literature, and these apparently increased communications may be due to a number of factors, including our institution's robust survivorship program and well established partnership with a community fertility clinic. Schover et al. [11] found that although over 90% of oncologists agreed that all male patients at risk for infertility should be offered sperm banking, only 52% discussed sperm banking with their patients (based on oncologist report). Furthermore, many young male cancer patients reported having no recollection of being told about the risks of infertility as a side effect of cancer treatment, nor of being provided with referrals to bank sperm [1,5,12]. It may be that increased anxiety at cancer diagnosis precludes patients and/or their family from hearing messages of infertility risk, as concerns at this time typically relate to mortality risk rather than survivorship issues. Indeed, adolescents with cancer as well as their parents often have misperceptions about their risk for infertility, so that those who are at low risk may suffer unnecessary anxiety about infertility whereas those at higher risk may not realize the importance of addressing fertility issues before or during their treatment [13].

These data support the need for interventions designed to increase sperm banking in this population, with potential targets of intervention being context and content of the messages provided by oncologists and other health care providers, as well as strategies to reduce anxiety and distress among families at or near diagnosis. These types of interventions may be warranted so that fertility-related messages can be truly understood by patients and their families, while efforts to preserve fertility in this group prior to cancer treatment can be acted upon in a timely manner. In pursuit of these goals, it would be helpful to assess the patients' and families' understanding of infertility-related risk soon after they are informed of the cancer diagnosis, but prior to the initiation of cancer treatment. A related goal would be to improve the knowledge of teens and their parents about the specific steps involved in sperm banking, including semen collection, cost of storage, and future use of assisted reproductive technology. Additional interventions that may improve rates of sperm banking might include the option of banking (to both in- and out-patients) within the confines of the treating institution, and presenting sperm banking as a standard practice to patients and families.

Of the medical variables considered in this study, we found that non-CNS solid tumor and CNS cancer patients were more likely to engage in sperm banking than leukemia/lymphoma patients. Alkylating agents like cyclophosphamide and ifosfamide, or combined alkylating agents therapies like MOPP (Methotrexate, Oncovin, Procarbazine, and Prednisone), have a dose-related risk of infertility with higher cumulative dose and longer length of treatment conferring the greatest risk for fertility problems [14–16]. This dose dependent relationship is also true in regard to radiation therapy as higher exposures translate to greater risk of gonadal dysfunction in both men and women [15]. The reduced utilization of sperm banking in the leukemia/lymphoma group may be due to the relatively reduced infertility risk that leukemia patients initially experience based on their proposed treatment, which can include lower cumulative doses of alkylating agents compared to the regimens used for the treatment of pediatric solid tumors. Yet, Tournaye et al. (2004) [17] pointed out that an initial low-risk treatment (in the case of acute lymphocytic leukemia, for example) may later change to one carrying a higher risk of infertility (i.e. transplant, second malignant neoplasm, relapse, etc.). Thus, all post-pubertal boys should be offered sperm cryopreservation, not just those considered at immediate or high risk for infertility at treatment initiation.

Although there has been a paucity of research on the utilization of fertility preservation options in underserved populations, our study found that lower SES was associated with decreased rates of sperm banking. One reason that sperm banking may be underutilized among those of lower SES could relate to the financial costs associated with sperm banking and storage [4]. Because our institution covers much of the initial sperm banking costs (e.g. history and physical, laboratory screening for sexually transmitted diseases, and initial semen analysis), the primary expenses which must be paid by the patients and their families include the preparation and freezing/storing of their child's sperm. Despite this financial assistance, there may be other factors associated with lowered SES which may affect sperm banking practices. For example, groups such as low SES African-Americans may distrust the medical community due to historical mistreatment (e.g., Tuskegee experiment) [4]. Additionally, infertility treatment may not be considered as important by low SES groups, who may not place as much significance on having biological offspring and have culturally sanctioned alternatives. For example, African-Americans frequently informally or formally adopt children, especially children of relatives [4]. These issues need to be explored in future studies that better evaluate the mechanisms motivating decisions for banking/not banking in low SES groups.

Within this group of teens and young adults, older patients tended to be more likely to sperm bank than younger patients. Although this difference did not reach statistical significance (likely due to lack of power), it is consistent with previous research and reinforces the notion that adolescent male cancer patients (particularly young adolescents) face difficult issues which

must be considered within the sperm banking context. In order to engage in fertility preservation procedures, adolescent patients must have reached puberty, though there are some experimental techniques for collecting sperm among prepubertal boys [17,18]. Additionally, many young adolescents have not yet considered whether or not they may want children in the future and may have trouble thinking realistically about possible infertility and its consequences. This is made much more difficult for adolescents with cancer, as they are suddenly facing a life-threatening disease that becomes a priority in their life and interrupts progression towards obtaining more normative medium and long term goals. In fact, female adolescents and parents have been found to be interested in fertility preservation, but are not willing to postpone cancer treatment to complete the requisite procedures [5]. Although males do not face the same time constraints as females in regard to engagement in fertility preservation procedures (i.e. weeks of hormone therapy, invasive harvesting, etc.), this is a complex issue that many teens are unprepared to consider at the time of cancer diagnosis.

Regarding religious affiliation, only one out of 18 Evangelical patients banked sperm. This finding was somewhat unexpected, as the use of fertility preservation techniques is not specifically prohibited by the leadership of these religious organizations. However, this may reflect moral concerns that are common among individuals belonging to these religions. For example, Evangelical churches often believe that life begins at conception and thus object to the possible fertilization of eggs that are not subsequently used for implantation, as is frequently the case with in vitro fertilization. Additionally, Evangelicals may object to masturbation, even to collect a sperm sample for assistance in reproduction.

Limitations to this study include a small sample size, which limits the generalizability of results, and possible problems with our measurement. For example, we relied on oncologists' reports to accurately identify who is and is not at risk for fertility problems based on proposed cancer treatment, while at the same time utilizing physician self-reports as to whether discussions of fertility risk occurred, and whether patients sperm banked or not. An alternate method would have been to ask the patients (or their parents) about these topics as opposed to relying exclusively on oncologist report. We were not able to ascertain, for example, if specific referrals to bank sperm were made by the medical team or if any patients attempted to bank but were unsuccessful. Another limitation is that many other factors contribute to whether or not one banks sperm which were not evaluated: medical factors (cancer site, quality of sperm at diagnosis), psychological factors (knowledge, risk perceptions, patient and familial attitudes regarding fertility), logistic factors (financial barriers, timing of sperm banking) and familial factors (discomfort in parent/child communication about sex/masturbation). It is clear that there are many advantages to sperm banking in this population and its underutilization makes this area a critical one for intervention.

The American Society of Clinical Oncology asserts that oncologists have a responsibility to discuss infertility risks due to cancer treatment with patients, taking into account factors such as age, disease, treatment type, and pretreatment fertility [10]. With the advancement of assisted reproductive technologies, preservation of fertility among childhood cancer patients will continue to be a priority not only for male teenagers, but for prepubertal boys and for females as well. In our roles as health care providers within the oncofertility context, it is critical that we not only provide timely and accurate infertility risk information in an easily understandable manner to all patients, but also to ensure that patients are aware of the concrete steps needed to preserve their fertility. Additionally, reducing logistical barriers, such as providing sperm collection sites within pediatric hospital settings, would likely increase utilization of banking. By taking these actions, we will maximize the likelihood that survivors of childhood cancer will continue to have viable fertility options in the future.

Acknowledgments

Supported in part by the American Lebanese Syrian Associated Charities (ALSAC), United States Public Health Service Cancer Center Support Grant CA21765, and Program Project Grant CA23099.

The authors would like to thank Drs. Leslie Schover, Eric Huyghe, and Dan Green for their thoughtful reviews of early drafts of this manuscript.

References

1. Schover LR, Brey K, Lichtin A, et al. Knowledge and experience regarding cancer, infertility, and sperm banking in younger male survivors. *J Clin Oncol* 2002;20(7):1880–1889. [PubMed: 11919248]
2. Neal MS, Nagel K, Duckworth J, et al. Effectiveness of sperm banking in adolescents and young adults with cancer: a regional experience. *Cancer* 2007;110(5):1125–1129. [PubMed: 17647219]
3. Schover LR, Rybicki LA, Martin BA, et al. Having children after cancer. A pilot survey of survivors' attitudes and experiences. *Cancer* 1999;86(4):697–709. [PubMed: 10440699]
4. Jenkins RL. Ensuring access to education and services on infertility for the underserved. *J Natl Cancer Inst Monogr* 2005;(34):101–103. [PubMed: 15784836]
5. Burns KC, Boudreau C, Panepinto JA. Attitudes Regarding Fertility Preservation in Female Adolescent Cancer Patients. *Journal of Pediatric Hematology and Oncology* 2006;28(6):350–354.
6. Langeveld NE, Grootenhuis MA, Voute PA, et al. Quality of life, self-esteem and worries in young adult survivors of childhood cancer. *Psychooncology* 2004;13(12):867–881. [PubMed: 15386796]
7. Glaser AW, Phelan L, Crawshaw M, et al. Fertility preservation in adolescent males with cancer in the United Kingdom: a survey of practice. *Arch Dis Child* 2004;89(8):736–737. [PubMed: 15269072]
8. Hollingshead, AB. Four factor index of social status. Department of Sociology, Yale University; New Haven, CT: 1975.
9. Institute for the Study of American Evangelicals (ISAE). Defining Evangelicalism [Web page]. Wheaton, IL: The Institute; 2006 [Accessed April 20, 2008]. Available at http://www.wheaton.edu/isae/defining_evangelicalism.html
10. Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006;24(18):2917–2931. [PubMed: 16651642]
11. Schover LR, Brey K, Lichtin A, et al. Oncologists' attitudes and practices regarding banking sperm before cancer treatment. *J Clin Oncol* 2002;20(7):1890–1897. [PubMed: 11919249]
12. Zebrack BJ, Casillas J, Nohr L, et al. Fertility issues for young adult survivors of childhood cancer. *Psychooncology* 2004;13(10):689–699. [PubMed: 15386645]
13. Oosterhuis BE, Goodwin T, Kiernan M, et al. Concerns about infertility risks among pediatric oncology patients and their parents. *Pediatr Blood Cancer* 2008;50(1):85–89. [PubMed: 17514741]
14. Kenney LB, Laufer MR, Grant FD, et al. High risk of infertility and long term gonadal damage in males treated with high dose cyclophosphamide for sarcoma during childhood. *Cancer* 2001;91(3):613–621. [PubMed: 11169946]
15. Bahadur G. Fertility issues for cancer patients. *Mol Cell Endocrinol* 2000;169(1–2):117–122. [PubMed: 11155943]
16. Meistrich ML, Wilson G, Brown BW, et al. Impact of cyclophosphamide on long-term reduction in sperm count in men treated with combination chemotherapy for Ewing and soft tissue sarcomas. *Cancer* 1992;70(11):2703–2712. [PubMed: 1423201]
17. Tournaye H, Goossens E, Verheyen G, et al. Preserving the reproductive potential of men and boys with cancer: current concepts and future prospects. *Hum Reprod Update* 2004;10(6):525–532. [PubMed: 15319377]
18. Keros V, Hultenby K, Borgstrom B, et al. Methods of cryopreservation of testicular tissue with viable spermatogonia in pre-pubertal boys undergoing gonadotoxic cancer treatment. *Hum Reprod* 2007;22(5):1384–1395. [PubMed: 17259225]

Table 1
Demographic, medical and religious characteristics of male patients 13 years of age and older.

	Total N = 66	At Risk N = 34	Banked Sperm N = 9 (26.5%)*	Did not Bank Sperm N = 25 (73.5%)	P-value
Age at diagnosis <i>M (SD)</i>	16.63 (2.37)	17.25 (2.28)	18.45 (2.88)	16.81 (1.91)	.064
<u>Race</u>					.092
Caucasian	41 (62.1%)	21 (61.8%)	5 (55.6%)	16 (64.0%)	
African-American	19 (28.8%)	9 (26.5%)	1 (11.1%)	8 (32.0%)	
Latino	3 (4.5%)	3 (8.8%)	2 (22.2%)	1 (4.0%)	
Multiracial	3 (4.5%)	1 (2.9%)	1 (11.1%)	0 (0%)	
<u>Religion</u>					.003 ^a
Catholic	11 (16.7%)	3 (8.8%)	2 (22.2%)	1 (4.0%)	
Evangelical	35 (53.0%)	18 (52.9%)	1 (11.1%)	17 (68.0%)	
Other Christian	14 (21.2%)	9 (26.5%)	3 (33.3%)	6 (24.0%)	
Jewish	1 (1.5%)	1 (2.9%)	1 (11.1%)	0 (0%)	
None listed	5 (7.6%)	3 (8.8%)	2 (22.2%)	1 (4.0%)	
<u>SES</u>					.031
Low SES	29 (43.9%)	18 (52.9%)	2 (22.2%)	16 (64.0%)	
High SES	37 (56.1%)	16 (47.1%)	7 (77.8%)	9 (36.0%)	
<u>Disease</u>					.013 ^b
Solid tumor	19 (28.8%)	16 (47.1%)	7 (77.8%)	9 (36.0%)	
Leukemia/lymphoma	31 (47.0%)	14 (41.2%)	0 (0%)	14 (56.0%)	
CNS	16 (24.2%)	4 (11.8%)	2 (22.2%)	2 (8.0%)	

* 28.1% of those *informed* of their risk for infertility (9/32) banked sperm.

^a Evangelical participants were less likely to bank sperm compared to all other religions.

^b Patients with CNS malignancy and non-CNS solid tumor were more likely to engage in sperm banking than were leukemia/lymphoma patients.