Testicular Biopsy for Fertility Preservation in Prepubertal Boys with Cancer: Identifying Preferences for Procedure and Reactions to Disclosure Practices

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Purpose: Fertility preservation options are limited in prepubertal boys with cancer. Worldwide there has been growing interest in testicular tissue cryopreservation as a promising experimental strategy to address future infertility. We measured and compared parent, male cancer survivor and provider willingness to accept the risk of testicular biopsy among prepubertal boys with cancer, and identified reactions to disclosure practices.

Materials and Methods: We conducted a multicenter study that included 153 parents of prepubertal boys with cancer, 77 male survivors of childhood cancer and 30 oncology providers. The threshold technique was used to measure subject relative willingness to accept risk of testicular biopsy under 4 different aspects of care, ie chance of infertility, complications from biopsy, development of technology to use tissue and tissue storage cost. A total of 47 in-depth interviews were conducted to identify reactions to disclosure practices.

Results: A total of 52 survivors (67%), 22 providers (73%) and 110 parents (72%) selected to have testicular biopsy (vs no biopsy). Median minimum infertility risk to make biopsy worthwhile varied from 25% to 30% among the 3 respondent groups. Interviews revealed that some providers would not offer biopsy in cases of greater perceived risk than benefit, that parents preferred having information regardless of risk of infertility and that nondisclosure elicited adverse feelings from some parents.

Conclusions: Parents, survivors and providers were willing to accept risk of prepubertal testicular biopsy. Parental/survivor desire for information and provider decision not to disclose suggest that barriers to information delivery need to be addressed.

Key Words: biopsy, cryopreservation, fertility preservation, testicular neoplasms

Abbreviations and Acronyms

ASCO = American Society of Clinical Oncology

FP = fertility preservation

TBx = testicular biopsy

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Study received research ethics board approval from each participating institution.

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MANY pediatric cancer treatments impair potential future fertility.[1] As survival rates for children with cancer improve, fertility concerns become an increasingly relevant issue and source of distress impacting survivor quality of life.[2,3] Postpubertal adolescent boys have an opportunity

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to preserve fertility through cryopreservation of ejaculated sperm or testicular tissue, from which mature sperm can be extracted and later used for in vitro fertilization. In prepubertal boys testicular biopsy is technically feasible yet considered experimental as prepubertal testes contain only spermatogonial cells, which with current technology cannot be matured in vitro to yield sperm suitable for future in vitro fertilization. Thus, at this time there are no options to preserve the fertility of prepubertal boys embarking on cancer treatment.

Promising animal models demonstrate that the technology is emerging. However, there has been limited exploration in humans due to the paucity of available immature testicular tissue for study.[4–8] Institutions reporting TBx procedures in prepubertal boys document a 76% uptake and 93.5% acceptance rate in referred patients.[9–11] Factors influencing parental decisions have been identified.[9,10,12] However, systematic analyses of parent reported outcomes and acceptable levels of risk associated with biopsy are lacking.

Institutions worldwide are developing formal comprehensive FP programs, including experimental options for prepubertal boys. However, it remains unclear which patients should be offered TBx due to procedural risk and cost of storage, particularly considering the current uncertain prospect of tissue viability. Furthermore, it is uncertain what reactions parents will have to practitioners who choose not to offer an option of TBx in instances of greater perceived risk than benefit for patients. ASCO clinical practice guidelines recommend that FP options be discussed at the earliest possible opportunity, including information regarding methods available for children that remain investigational, and to "refer for experimental protocols when available."[13]

Based on these issues, we sought to measure the relative willingness of parents, male survivors of childhood cancer and providers to accept risk of TBx in varying conditions of care and to identify reactions to disclosure practices regarding biopsy. We hypothesized that all groups will accept baseline values for risks associated with biopsy, although the tolerance for risk beyond this point is uncertain.

METHODS

Study Participants

Participants included survivors and parents of boys with cancer who were 12 years or younger at diagnosis, had completed at least 2 months of therapy and either were still receiving active therapy or had completed therapy. All eligible parents and survivors were approached at ambulatory clinics between July 2012 and September 2013. Eligible providers worked exclusively in pediatric oncology and directly participated in disclosure of infertility risk and FP options. Three Canadian centers participated (Hospital for Sick Children, BC Children's Hospital and McMaster Children's Hospital). Survivors were adolescent males who had completed chemotherapy and were currently 14 to 25 years old. Patients who underwent bone marrow transplant (due to chemotherapy exposure before FP discussion) and families who did not speak English were excluded.

Overall Study Design

Research ethics board approval was obtained from each participating institution, and enrolled subjects provided informed consent. A prephase of in-depth interviews with 5 parents, 5 oncologists and 5 cancer survivors was conducted to identify the main conditions of care in FP decisions for later use in the threshold technique. Standardized scripts were used for the threshold technique measuring willingness to accept risk for biopsy and to inform an interview guide for in-depth dialogues identifying reactions to disclosure practices. A standardized 15-minute education session regarding FP preservation in prepubertal boys was completed before the threshold technique and interviews (supplementary Appendix 1).

Measuring Relative Willingness to Accept Risk for TBx

The threshold technique was followed to measure relative willingness to accept risk scores for TBx vs biopsy for prepubertal boys with cancer. These scores reflect how much risk a parent, survivor or provider would accept for TBx and thus the desirability or undesirability of TBx for potential FP. These scores were derived under 4 aspects of care, namely risk of infertility from chemotherapy, chance of complications from biopsy, likelihood that technology would be developed to use the tissue clinically once the patient became interested in reproduction and cost associated with testicular tissue storage. Baseline probabilities of the 4 conditions of care associated with TBx were set at clinically reasonable levels (50% for infertility, 1% for biopsy complications, 15% for development of tissue utilization technology and $350 yearly for storage cost).[1,4,6,7,14] High desirability for TBx was represented by willingness to accept lower risks of infertility, lower probabilities that technology would be developed, greater chances of complications from biopsy and higher costs of tissue storage. Supplementary Appendix 2 outlines the format of the threshold technique and scoring of the minimum and maximum acceptable risk scores.

Predicting Relative Willingness to Accept Risk for TBx Scores

Demographic data were analyzed to determine potential predictors of willingness to accept risk scores for TBx. For parents, survivors and providers a priori defined predictors included age, gender and ethnicity. Additional demographic data were tested for parents as they would be the primary decision makers regarding TBx for boys. These data included child age at treatment, yearly household income and underlying diagnosis.