

The role of sperm banking in fertility preservation

O.A. Olatunbosun, L. Zhu

Department of Obstetrics, Gynecology and Reproductive Sciences, University of Saskatchewan, Saskatoon, Saskatchewan (Canada)

Summary

Objective: To investigate factors that influence sperm banking before cancer therapy and assess the use and disposal of banked sperm after cancer treatment. **Study Design:** Database exploratory study combined with questionnaire survey of a cohort of 55 men who cryopreserved their sperm at an Andrology Clinic. **Main Outcome Measure(s):** Rate of use, disposal and abandonment of banked sperm, current fertility, and patient satisfaction with sperm banking. **Results:** Using logistic regression, we analyzed the factors associated with use and disposal of banked sperm, current fertility status, reproductive outcomes and quality of life in 55 survivors of cancer therapy who cryopreserved sperm at our facility. Most (93%) of the patients undergoing sperm banking before cancer treatment did not use their samples and 33% requested sperm disposal following completion of cancer therapy. Married status and fatherhood before cancer therapy were associated with higher rates of sperm disposal. Sperm disposal was requested because the subjects remained fertile, spontaneously fathered a child, or completed their family. The families of four patients (7%) who died from their cancer also requested disposal of the stored sperm. Six (11%) patients could not be located or failed to contact the clinic and were considered to have abandoned their banked sperm. Only 7% of the patients used their cryopreserved sperm for assisted reproduction. Most of the patients that banked sperm achieved pregnancy with their partners through spontaneous conception compared to through the use of cryopreserved sperm. **Conclusions:** The rates of disposal and abandonment of banked sperm were high following cancer therapy. Retention of fertility appears to contribute to the low utilization of banked sperm, which emphasizes the need for appropriate consent and directives regarding disposal of unused cryopreserved sperm.

Key words: Fertility preservation; Sperm banking; Sperm use and disposal.

Introduction

Therapeutic advances during the past decades have improved the long-term survival of patients with malignant diseases. The overall 5-year survival rate for cancer in young individuals has risen to 60%; the rates being much higher for Hodgkin's disease (82%) and testicular cancer (95%), two of the most common tumors in men in the reproductive age [1-7]. With increasing numbers of cancer survivors, quality of life issues are receiving more attention. Fertility is one of the major concerns of men and women surviving cancer. Cancer treatment, whether by surgery, radiotherapy or chemotherapy, can have severe and adverse long-term iatrogenic effects on male and female fertility. Chemotherapy and radiation therapy compromises fertility through their cytotoxic effects on gametogenesis. The degree of gonadotoxic effect is governed by the regimen used (i.e., type, dose, regimen) and duration of the treatment [8]. Further, men with newly diagnosed cancer often have poor semen quality that is associated with limited success in achieving pregnancy after semen banking and subsequent intrauterine insemination. In addition, the process of cryopreservation results in further reduction in semen quality. Fertility may return after cancer treatment in some but not in all individuals, and who will be affected cannot be predicted. For some patients, a method to preserve fertility potential is feasible. Therefore, patients need to be counseled on fertility-sparing opportunities before commencing potentially sterilizing cancer regimens.

The present clinical means for preserving the potential reproductive capacity of men at risk is cryopreservation of sperm before the treatment begins, followed by artificial insemination or assisted reproductive techniques (ART) when pregnancy is desired. Because most reports that have been published focus on fertility outcomes with assisted reproduction using cancer patients' cryopreserved sperm [8-11], there is inadequate information to guide patient counseling to encourage sperm banking particularly for those with advanced cancer and poor semen quality that may not be suitable for cryopreservation. Preserving the fertility of younger, prepubertal patients raises special concerns about the welfare of offspring resulting from an expected reduced life span of the parent [12]. Further, ethical issues regarding the disposal of the frozen semen and the use of sperm posthumously raise ethical and emotional issues that have not been sufficiently addressed [13, 14]. The aim of this study was to investigate factors that influenced sperm banking at our center. We also sought to elucidate factors associated with disposal of banked sperm by young individuals diagnosed with cancer. Our study sought to provide insights into the rationale for sperm storage from the perspective of patients that may guide the reproductive care of young men with cancer.

Methods

Participants in this study were 70 males diagnosed with malignant diseases and referred for sperm banking at the Andrology Clinic of the Department of Obstetrics, Gynecology and Reproductive Sciences at the Royal University Hospital, Saskatoon, during a 13-year period (1991 to 2004), before

undergoing surgery, chemotherapy or radiotherapy for their cancer. A detailed database of clinical and sperm variables has been maintained in our unit since 1990. At referral, semen analysis was done to assess pretreatment alterations in sperm numbers, motility and post-thaw motility recovery that influenced the likelihood of successful cryopreservation. The patients signed written consent for sperm banking including indicating their preferences for sperm disposal in the event of death. Patients were followed by the cancer centers to monitor their cancer status, were advised to be in contact with the Andrology Clinic and were sent annual notification concerning continuation or disposition of their cryopreserved sperm.

Following approval from the University of Saskatchewan Human Research Ethics Committee, a consent form explaining the purpose of the study and a questionnaire were mailed to the participants. This was followed by attempts at contacting the patients by telephone. The medical records of all the patients who banked sperm were reviewed. Demographic and clinical data reviewed included age, marital status, cancer diagnosis, modality of cancer treatment, reasons for sperm banking, semen quality, number of banked sperm samples, date of sperm banking, reasons for and date of sperm disposal, and use of frozen sperm. In addition, the outcomes of cancer therapy, current fertility and fatherhood status, and overall satisfaction with sperm banking were evaluated.

Quantitative indices

A University of Saskatchewan Fertility after Cancer (USASK-FAC) questionnaire was designed by the authors to evaluate the role of sperm banking in fertility preservation for patients diagnosed with cancer. There were 12 questions in the questionnaire, categorized into three groups: pre-cancer, post-cancer and future, as illustrated in Table 1. The first four questions were related to the time period before sperm banking and cancer treatment, while questions 5 through 9 were designed for the post-treatment follow-up period. The last three questions (10 through 12) were used to identify patient intentions regarding use or disposal of their banked sperm samples. Each question was evaluated by one or two numerical numbers that represented different choices associated with that question.

Statistical analysis

All data were stored in an information database and were analyzed using commercial software (SPSS, Chicago, IL). Descriptive statistics were used to characterize the baseline information and to elucidate the information described in the introduction section. Histograms or pie charts were used to show the utilization frequency or the outcomes of sperm banking in clinical practice. The correlation between important factors in sperm banking was assessed using cross-table analysis and chi-square measures. Discriminate analysis was used to investigate the effects of multiple factors, four in this study, on conception or birth after cancer treatment.

Results

Fifty-five of the 70 (78.5%) patients who were referred by their cancer specialists to our Andrology Clinic completed sperm banking. The patients varied in age from 15 to 46 years, with a mean age of 34 years and standard deviation of 4.7 years. Fifteen patients were excluded

Table 1. — *University of Saskatchewan fertility after cancer questionnaire.*

Questions	Score range
1. Marital status before cancer diagnosis	1 through 4
2. Number of children before cancer diagnosis	1 through 10 or Binary
3. Plan for future parenthood the time of sperm banking	1 through 3
4. Reasons for sperm banking	1 through 5
5. Marital status after cancer treatment	1 through 4
6. Attempted conception after cancer treatment	Binary
7. Spontaneous conception after cancer treatment	1 through 6
8. Conception using assisted reproduction after cancer treatment	1 through 6
9. Reasons for disposal of banked sperm	1 through 13
10. Future intention of using samples	1 through 3
11. Future direction of banked sperm in case of death	1 through 4
12. Overall experience with sperm banking	1 through 10

Table 2. — *Chi-Square tests for the role of "children before cancer" in achieving pregnancy after cancer treatment.*

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson chi-square	3.853 ^b	1	.050		
Continuity correction ^a	2.379	1	.123		
Likelihood ratio	3.660	1	.056		
Fisher's exact test				.090	.064
Linear-by-linear association	3.754	1	.053		
N of valid cases	39				

^aComputed only for a 2x2 table

^b1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.67.

from the survey. These included five patients who had already had surgery and chemotherapy and were excluded because their semen samples were inadequate for cryopreservation. Four patients who were too ill to produce samples for initial semen analysis were excluded. Another four patients who were offered the service declined sperm banking for personal reasons. Two pre-pubertal boys were excluded for lack of sperm samples. The clinical records of the 55 patients were reviewed and the USASK-FAC questionnaire was sent to each of the patients by registered mail with stamped return envelopes. A response rate of 54.5% (30 of 55 participants) was achieved through this postal survey. An additional 15 responses were obtained through follow-up telephone inquiry, for an overall response rate of 81.8% (45 of 55 participants). Ten patients could not be directly reached and four of the patients (7.3%) were known to be diseased. Six patients (11%) that could not be reached were deemed to have been lost to follow-up and were considered to have abandoned their cryopreserved sperm. Considering the time span that was reviewed in this study, it is possible that some of the patients that could not be reached were also no longer alive.

On the basis of the patients' information in the questionnaire and their clinical records, we organized our findings into the following two groups, which represent different time lines in the process of cancer treatments.

Fig. 1

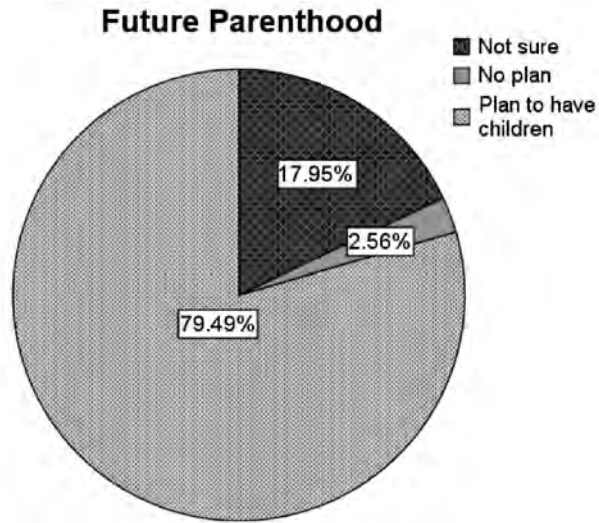


Fig. 2

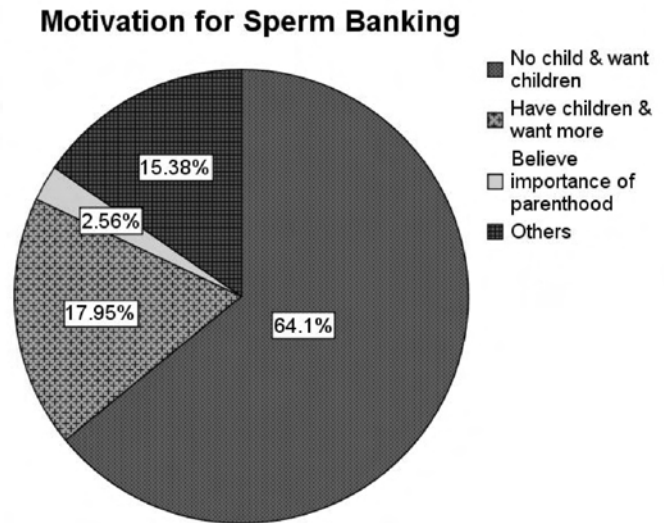


Fig. 3

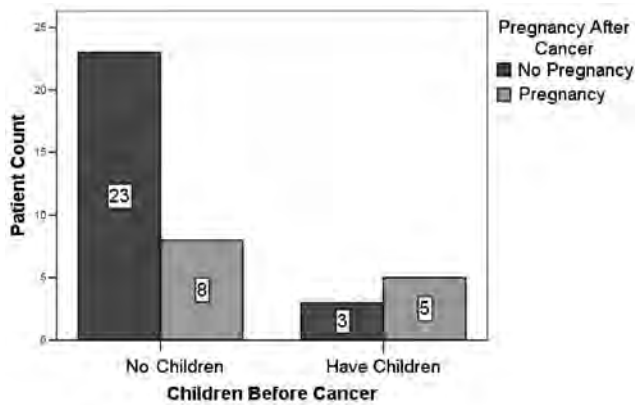


Fig. 4

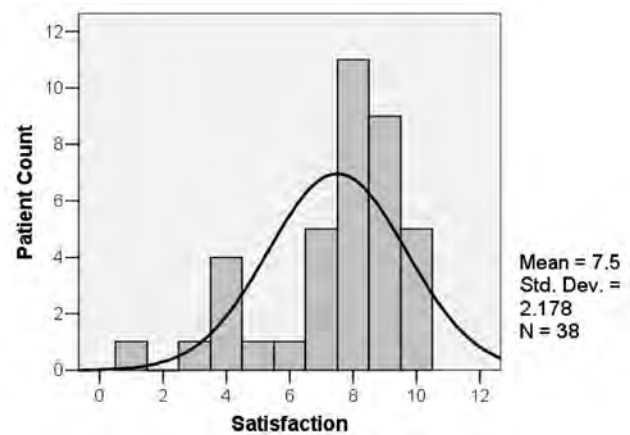


Figure 1. — Intentions of patients about future plans for parenthood before sperm banking.

Figure 2. — Distribution of patients' reasons for sperm banking.

Figure 3. — The role of "children before cancer" in achieving pregnancy after cancer treatment.

Figure 4. Histogram of patients' overall experience with sperm banking (1 – low level of satisfaction through 10 – extremely satisfied).

Rationale for sperm banking before cancer treatment

In the USASK-FAC questionnaire, there were two questions (3 and 4 in Table 1) related to patients' reasons for seeking sperm banking. Figure 1 demonstrates that more than 80% of patients intended to have children in future after cancer treatment, and only 2.6% of patients did not plan to. The remaining 18% of patients were unsure about future parenthood. One possible reason is that some of these patients were still very young and uncertain of future desires regarding parenthood. The pie chart in Figure 2 reveals different reasons that patients had for choosing sperm banking. A large proportion of patients (82%) sought sperm banking because of their interest in future parenthood after cancer therapy. Of these, 64% have not fathered a child at the time of cancer diagnosis and another 18% of patients who had children wanted more after cancer treatment.

Use and disposal of banked semen following cancer treatment

The utilization of banked sperms presents an interesting finding. Of the 55 patients who banked their sperm, only four (7.3%) who were not parents before cancer treatment used their cryopreserved sperm for assisted reproduction (3 for artificial insemination and 1 for in vitro fertilization). Two of these were successful. Approximately 93% of patients did not make use of their cryopreserved sperm. Fourteen patients (25.5%) achieved spontaneous conception after cancer therapy without using their banked sperm samples. The time interval from treatment to conception varied from one to eight years. Only ten patients (18.2%) used follow-up semen analysis to ascertain their fertility potential following cancer therapy. Of these patients, three had azoospermia, two had oligozoospermia, and five had normal semen parameters. Eighteen (32.7%) of the patients requested disposal

of their sperm samples because they remained fertile, spontaneously fathered a child or completed their family.

We attempted to elucidate the factors that influenced the possibility of pregnancy or birth after cancer treatment. Figure 3 shows that having “children before cancer” treatment was a strong indicator for achieving pregnancy after cancer treatment. It could be inferred that if a patient had children before cancer treatment, he would likely be more successful in achieving a pregnancy with his partner after cancer treatment. On the contrary, only one in four patients achieved a pregnancy if they had no children before cancer treatment. A crosstabs analysis in Table 2 shows that p value of the Pearson chi-square (asymptotic significance) is just around the threshold of statistical significance (i.e., $p = 0.05$). This suggests that having “children before cancer” treatment has a strong correlation with achieving pregnancy after cancer treatment.

Figure 4 presents the overall satisfaction with the sperm banking service, in which we use a ten-point grading system to assess the level of satisfaction. Grade 1 refers to very low level of satisfaction while grade 10 means a high level of satisfaction. Average satisfaction of patients who chose the banked sperm service was 7.5 with a standard deviation of 2.2. Overall, 65% of patients were satisfied with current sperm banking services.

Discussion

We found a high rate of request for disposal of cryopreserved sperm following cancer therapy because most patients remained fertile. Rates of sperm disposal were highest among patients who were either married or were parents at the time of sperm banking. The rate of abandonment of banked sperm was highest among those who were single.

Long-term sperm banking began in our Andrology Clinic in 1990. This study reported our experience with 55 patients who banked their sperm samples up to 2004. The results of this study demonstrate that the majority of patients accepted sperm banking as important to preserving their fertility before cancer therapy. The key motive that seems to guide the decision for semen cryopreservation is ensuring the opportunity for biological parenthood and not risking the prospect of sterility. One important finding in this study is the contradiction between high motivation for sperm banking, the low rate of utilization for subsequent reproduction and high rate of request for disposal of the cryopreserved semen. While on the one hand a majority of patients had a strong interest in sperm banking, on the other hand, the same group of patients rarely utilized their banked sperm for subsequent reproduction. This fact raises a question about the practical utility of sperm banking in the overall management of patients with malignant diseases.

Considerable difficulty was encountered in the follow-up of patients banking semen before cancer therapy. Consistent with earlier studies, a substantial number (11%) of our patients who consented to semen cryopreservation and indicated interest in future reproduction failed to

maintain contact with the Andrology Clinic and could not be contacted to make their wishes known regarding continued storage or disposition. This raised the question of whether to consider that the banked semen has been abandoned and poses an ethical dilemma regarding their disposition or continued storage. Because of legal uncertainty and a lack of clear guidance on this issue, our practice is to continue indefinite storage. The Ethics Committee of the American Society for Reproductive Medicine is of the opinion that gametes or embryos deemed abandoned should not be donated to other couples or used for research without prior consent [15].

Our results suggest that several factors may have influenced the utilization of cryopreserved sperm after the cancer treatment. These include marital status prior cancer therapy, paternity before cancer diagnosis and treatment, fertility status following cancer therapy and general health and cancer survivor status.

More patients achieved pregnancy or birth though spontaneous conception as compared to the use of banked semen. The ratio between these two groups is about one in ten, that is, for every patient who achieved the pregnancy or birth by utilizing the banked sperms, there are ten patients who succeeded in pregnancy or birth through the spontaneous conception after the cancer treatments.

Our findings would suggest that patients who are married or have fathered a child prior to cancer therapy have a higher likelihood of achieving fatherhood after cancer treatment, regardless of whether or not sperm banking service is used. On the contrary, patients who have not fathered a child prior to cancer therapy had a reduced likelihood of achieving a conception with their partner after cancer treatment. Therefore, it is important to consider sperm banking for to this group of patients prior to cancer treatment.

Our study has certain limitations including the short follow-up period. Further, the views and reproductive outcomes of the substantial numbers of patients that we were unable to reach might differ from those of the respondents and influence the overall findings. In addition, the questionnaires addressed reproductive issues that some might consider too personal to elicit elaborate responses. These limitations notwithstanding, the results from this study are striking, particularly in their demonstration of the substantial proportion of patients who requested disposal of their banked sperm following cancer treatment, the substantial number of patients who remained fertile and achieved spontaneous conception, and the high frequency of abandonment of banked sperm. These results emphasize the need for adequate counseling before sperm banking and provision of clear directives regarding sperm disposition after cancer treatment.

Acknowledgements

This study was supported by the University of Saskatchewan College of Medicine Clinical Teaching and Research Grant. The authors would like to express their gratitude to Ms. Audrey Eby Senior Andrology Laboratory technologist for providing the Sperm Banking Database.

References

- [1] Anger J.T., Gilbert B.R., Goldstein M.: "Cryopreservation of sperm: indications, methods and results". *J. Urol.*, 2003, 170, 1079.
- [2] Lamar C.A., DeCherney A.H.: "Fertility preservation: state of the science and future research directions". *Fertil. Steril.*, 2009, 91, 316.
- [3] Styer A.K., Cekleniak N.A., Legedza A., Mutter G.L., Hornstein M.D.: "Factors associated with disposition of cryopreserved reproductive tissue". *Fertil. Steril.*, 2003, 80, 584.
- [4] Schuster T.G., Hickner-Cruz K., Ohl D.A., Goldman E., Smith G.D.: "Legal considerations for cryopreservation of sperm and embryos". *Fertil. Steril.*, 2003, 80, 61.
- [5] Williams D.H.: "Sperm banking and the cancer patient". *Therap. Advanc. Urol.*, 2010, 2, 19.
- [6] Ragni G., Somigliana E., Restelli L., Salvi R., Arnoldi M., Paffoni A.: "Sperm banking and rate of assisted reproduction treatment: insights from a 15-year cryopreservation program for male cancer patients". *Cancer*, 2003, 97, 1624.
- [7] Lysterly A.D., Nakagawa S., Kuppermann M.: "Decisional conflict and the disposition of frozen embryos: implications for informed consent". *Hum. Reprod.*, 2011, 26, 646.
- [8] Agarwal A., Ranganathan P., Kattal N., Pasqualotto F., Hallak J., Khayal S., Mascha E.: "Fertility after cancer: a prospective review of assisted reproductive outcome with banked semen specimens". *Fertil. Steril.*, 2004, 81, 342.
- [9] Bredkjaer H.E., Grudzinski J.G.: "Cryobiology in human assisted reproductive technology. Would Hippocrates approve?". *Early Pregn.*, 2001, 5, 211.
- [10] Bahadur G., Whelan J., Ralph D., Hindmarsh P.: "Gaining consent to freeze spermatozoa from adolescents with cancer: legal, ethical and practical aspects". *Hum. Reprod.*, 2001, 16, 188.
- [11] van der Kaaij M., van Echten-Arends J., Simons A.H.M., Kluin-Nelemans H.C.: "Fertility preservation after chemotherapy for Hodgkin lymphoma". *Hematol. Ontol.*, 2010, 28, 168.
- [12] Sauvat F., Binart N., Poirot C., Samacki S.: "Preserving fertility in prepubertal children". *Horm. Res.*, 2009, 71 (suppl. 1), 82.
- [13] ESHRE taskforce on ethics and law "Taskforce 7: Ethical considerations for the cryopreservation of gametes and reproductive tissues for self use". *Hum Reprod.*, 2004, 19, 460.
- [14] Deepinder F., Agarwal A.: "Technical and ethical challenges of fertility preservation in young cancer patients". *Reprod. BioMedic. Online*, 2008, 16, 784.
- [15] Ethics Committee of the American Society for Reproductive Medicine: "Disposition of abandoned embryos". *Fertil. Steril.*, 2004, 82, S253.

Address reprint requests to:
 O.A. OLATUNBOSUN, M.D.
 Department of Obstetrics, Gynecology &
 Reproductive Sciences
 College of Medicine
 University of Saskatchewan
 Royal University Hospital
 103 Hospital Drive
 Saskatoon Saskatchewan S7N 0W8 (Canada)
 e-mail: femi.olatunbosun@usask.ca