Sperm banking for fertility preservation: a 20-year experience

Matrika D. Johnson a,*, Amber R. Cooper b, Emily S. Jungheim b, Susan E. Lanzendorf b, Randall R. Odem b, Valerie S. Ratts b

a Division of Reproductive Endocrinology and Infertility, Department of Obstetrics, Gynecology & Reproductive Sciences, Magee-Womens Hospital of UPMC, 300 Halket Street, Pittsburgh, PA 15213, USA

b Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Washington University School of Medicine in St. Louis, 4444 Forest Park Avenue, Suite 3100, St. Louis, MO 63108, USA

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A B S T R A C T

Objective: Sperm banking is an effective method to preserve fertility, but is not universally offered to males facing gonadotoxic treatment in the United States. We compared the disposition and semen parameters of cryopreserved sperm from individuals referred for sperm banking secondary to a cancer diagnosis to those of sperm from men banking for infertility reasons.

Study design: We performed a retrospective cohort study that reviewed 1118 records from males who presented to bank sperm at Washington University between 1991 and 2010. We collected and analyzed demographics, semen parameters, and disposition of banked sperm.

Results: Four hundred and twenty-three men with cancer and 348 banking for infertility reasons attempted sperm cryopreservation in our unit during the specified time period. The most prevalent cancers in our cohort were testicular (32%), lymphoma (25%), and leukemia (11%). Patients with leukemia had the lowest pre-thaw counts and motility. Most cancer patients (57%) who banked elected to use, transfer to another facility, or keep their specimens in storage. The remaining samples were discarded electively (34%) or following death (8%). Overall semen parameters were similar between the cancer and infertility groups, but demographics, ability to bank a sample, azoospermia rates, length of storage, current banking status, and use of banked sperm differed significantly between the two groups.

Conclusions: The majority of cancer patients who banked survived their cancer and chose to continue storage of banked samples. Cancer patients were more likely than infertility patients to use or continue storage of banked samples. Our study provides evidence that sperm banking is a utilized modality of fertility preservation in patients with a myriad of cancer diagnoses and should be offered to all men facing gonadotoxic therapies. Further work is needed to determine where disparities in access to sperm banking exist to improve the potential for future fertility in these males.

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1. Introduction

In 2012, over 848,000 new cancers were diagnosed in male patients in the United States (U.S.) [1]. With advancing technology in chemotherapeutic agents and radiation, the overall survival rate of patients treated for many types of cancer has improved from 50% in the 1970s to nearly 70% in the 1990s, and the current cure rates for patients with testicular cancer and lymphoma can be as high as 90% [1].

These successes have led to efforts to improve the quality of life after treatment. Because approximately 15–30% of cured cancer patients become infertile as a consequence of treatment, attention has turned to the preservation of reproductive function [2]. In male patients, sperm banking before cancer treatment is considered the most effective method to preserve fertility [3,4]. Therefore, in 2005, the American Society of Reproductive Medicine Ethics Committee and the American Society of Clinical Oncology both recommended that physicians inform all cancer patients about options for fertility preservation before treatment [5–7].

Despite these recommendations, oncologists do not universally offer fertility preservation options to patients. One survey revealed that although 91% of U.S. oncology fellows and oncologists agree that sperm banking should be offered to all male cancer patients, 48% admit to never discussing it or mentioning it to less than 25% of eligible patients [8]. Recent efforts are attempting to address this situation. For example, in 2012 Sheth et al. reported that implementation of a formal fertility preservation consultation program increased the frequency of service offerings to male patients.
cancer patients aged 18–40 from less than 10% in 2002 to more than 40% in 2010 [9].

Both physicians and cancer patients appear to be unaware of the opportunities for sperm cryopreservation that are available. A few studies have attempted to address this issue by performing demographic analyses of the oncology patients who bank their sperm and the disposition of the samples after 10–20 years in storage, asking such questions such as: which cancer types are represented by those who bank? What fraction of men use, continue to store, or discard their stored sperm? Can adolescents successfully provide samples? What is the quality of the sperm pre- and post-storage? Only two of these studies [9,10] were performed at university associated fertility clinics in the U.S., so an important question is whether their findings can be extrapolated to other sites.

Since January 1991, the Division of Reproductive Endocrinology and Infertility at Washington University in St. Louis has been offering sperm banking to patients facing potentially sterilizing therapy. The primary objective of our study was to evaluate the dispositions of the cryopreserved samples in our 20-year experience of sperm banking, to provide further epidemiological information about the utility of sperm cryopreservation in the U.S. Our secondary objective was to compare the sperm parameters of cancer patients to those of men banking sperm for infertility reasons.

2. Materials and methods

2.1. Patients

The Washington University School of Medicine’s Human Research Protection Office and Barnes-Jewish Hospital’s Alvin J. Siteman Cancer Center Protocol Review and Monitoring Committee approved the protocol before the study began. Medical records of all patients who attempted sperm banking at Washington University from January 1, 1991 to February 1, 2010 were reviewed. Patients who banked samples after testicular sperm extraction (TESE) were excluded.

The following information was extracted from charts: age; marital status (married or not married, which included single, engaged, divorced, or widowed); banking indications; cancer type, stage, grade, and treatment, if known; reasons for failure to bank (including failure to produce a sample, azoospermia, and poor quality semen sample); pre- and post-thaw sperm counts and motility; disposition of cryopreserved sperm; current banking status; and length of storage. The disposition categories were failure to bank, shipped, used in our unit, ongoing storage within our unit, electively discarded, and discarded secondary to death. (In our clinic, it is customary that men designate the disposition of their cryopreserved sperm in the event of their death. All discards were at the request of the patients or the patient-assigned custodians of the specimens.) Banking status was defined as active if patients had a cryopreserved sample as of February 1, 2010 and inactive if they had used or discarded all samples by that date. Length of storage was the number of days from the time the first sample was banked to the time the last sample was used or discarded or to February 1, 2010.

2.2. Semen samples

Before banking, all patients were provided with a consent form and information packet that discussed the medical indications for banking; STD testing, semen collection, and

![Fig. 1. Flow diagram of men who presented to Washington University in St. Louis from 1991 to 2010 for sperm cryopreservation. TESE, testicular sperm extraction; MESA, microsurgical epididymal sperm aspiration; NHL, non-Hodgkin lymphoma.](image-url)
abstinence requirements; and procedures for future use of the specimens. Patients were informed that a small portion of the sample would be thawed for analysis to counsel patients on the number of samples to bank and potential uses of banked samples. Semen analyses were performed according to World Health Organization (WHO) recommendations in publications at the time the specimens were collected [11–13]. All samples were collected by masturbation. Cryopreservation and thawing of the spermatozoa was performed as previously described [14], with glycerol used as the cryoprotectant and chicken egg yolk as the extender [15]. Samples were cooled to −70 °C in a freezing rack at which time they were plunged and stored in liquid nitrogen. Thawing was performed by placing the cryovial in a beaker containing 30 °C water until all ice crystals had disappeared [14].

A diagnosis of azoospermia was given by classical analysis of the semen and confirmed by centrifugation of the entire semen sample. Between 1992 and 1999, 12 samples were not banked due to being deemed poor quality by a physician in our facility. The specific parameters were not available on the charts.

2.3. Statistical analysis

Continuous outcomes were analyzed by using Student’s t-test, one-way analysis of variance, Wilcoxon rank-sum test, or the Kruskal–Wallis test. Dichotomous outcomes were compared using Fisher’s exact or the Chi-square test. In all cases, p < 0.05 was considered statistically significant.

3. Results

3.1. Population studied

A total of 1118 patients attempted sperm cryopreservation between January 1991 and February 2010 (Fig. 1); 771 met the inclusion criteria for our study, and 347 were excluded. Of these, 212 were excluded for a banking indication other than cancer or infertility reasons. Exclusions included prior to vasectomy, for use as a directed donor, prior to non-cancer-related surgery, for partner’s use while patient was traveling, and for unknown indications. Because we only wanted to analyze data from patients presenting to our office to bank a semen sample, we were only interested in samples collected by masturbation in our facility, and we excluded 135 for banking TESE sperm. The cancer diagnoses of the 423 included patients were testicular (32%), lymphoma (25%), leukemia (11%), prostate (9%), sarcoma (5%), colorectal (5%), brain (4%), other (5%), and unspecified (4%) (Fig. 1). The “other” group was composed of bladder, skin, thyroid, renal, stomach, urachal, and urethral carcinomas, primitive neuroectodermal tumor, paraganglioma, sacral chordoma, a chest teratoma, myelodysplasia, and hemophagocytic lymphohistiocytosis.

The demographics of the cancer patients are listed in Table 1. Of the 423 cancer patients who requested banking, 378 (89%) successfully banked sperm between January 1, 1991 and February 1, 2010. Forty-five patients (11%) failed to bank a sample: 9 (2%) due to poor quality, 12 (3%) because they were unable to produce a sample by masturbation, 23 (5%) due to azoospermia, and 1 for an unspecified reason. The mean age in the group that produced a sample was 29.8 ± 10.5 years versus 20.8 ± 4.9 in the group that failed to produce a sample. The reasons for failure to bank did not differ significantly between the various cancer groups.

3.2. Semen parameters

Among the 378 cancer patients who banked, the median number of samples was one to two (range 1–18) in all cancer
Table 2
Characteristics of leukemia patients versus all other cancer patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Leukemia</th>
<th>Other cancers</th>
<th>p-Value ( ^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics ( ^a )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age at banking (years)</td>
<td>24.2 ± 6.3</td>
<td>30.4 ± 10.7</td>
<td>&lt;0.0001 ( ^e )</td>
</tr>
<tr>
<td>Mean age at death (years)</td>
<td>25.9 ± 7.5</td>
<td>30.6 ± 9.2</td>
<td>0.2 ( ^c )</td>
</tr>
<tr>
<td>Semen parameters with range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median # of samples banked</td>
<td>1 (1–7)</td>
<td>2 (1–18)</td>
<td>0.05 ( ^d )</td>
</tr>
<tr>
<td>Median pre-count (10^6/mL)</td>
<td>9.9 (0–546.0)</td>
<td>33.5 (0–518.6)</td>
<td>0.0007 ( ^d )</td>
</tr>
<tr>
<td>Median pre-motility (%)</td>
<td>17 (0–92)</td>
<td>44 (0–97)</td>
<td>0.0001 ( ^h )</td>
</tr>
<tr>
<td>Median post-count (10^6/mL)</td>
<td>5.3 (0.1–132.4)</td>
<td>16.3 (0–201.0)</td>
<td>0.001 ( ^i )</td>
</tr>
<tr>
<td>Median post-motility (%)</td>
<td>6 (0–59)</td>
<td>20 (0–82)</td>
<td>&lt;0.0001 ( ^d )</td>
</tr>
<tr>
<td>Banking information</td>
<td></td>
<td></td>
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<tr>
<td>Length of storage with range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median days banked</td>
<td>1128 (51–4606)</td>
<td>1436 (2–6970)</td>
<td>0.36 ( ^d )</td>
</tr>
<tr>
<td>Median days banked to death</td>
<td>336 (69–1037)</td>
<td>680.5 (47–3809)</td>
<td>0.02 ( ^d )</td>
</tr>
<tr>
<td>Banking outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discarded secondary to death, n (%)</td>
<td>11 (24)</td>
<td>21 (6)</td>
<td>&lt;0.0001 ( ^e )</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living, n (%)</td>
<td>24 (69)</td>
<td>322 (94)</td>
<td>&lt;0.0001 ( ^e )</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>11 (31)</td>
<td>21 (6)</td>
<td></td>
</tr>
</tbody>
</table>

\( ^a \) Values are mean ± SD.
\( ^b \) \( p < 0.05 \) significant.
\( ^c \) Student’s t-test was used.
\( ^d \) Wilcoxon rank-sum test was used.
\( ^e \) Chi-square test was used.

groups (Table 1). Before cryopreservation, the overall median sperm count was 31.6 \( 10^6/mL \) and motility was 43%. Post-thaw analyses after cryopreservation revealed a median count of 15.7 \( 10^6/mL \) and motility of 19%. There was no difference in change from pre- to post-thaw counts or motility between the various cancer groups. Semen parameters, however, did vary by cancer diagnosis (Table 1). Patients with leukemia had the poorest samples, with lower post-thaw counts and motility (Table 2). This was true when comparing leukemia patients to the lymphoma group (\( p = 0.001 \) and \( p = 0.0003 \), testicular cancer group (\( p = 0.02 \) and \( p = 0.0005 \), and all other cancers (\( p = 0.0007 \) and \( p = 0.0001 \)).

3.3. Disposition of cryopreserved sperm

A significant difference was seen in the disposition of the banked samples between the cancer groups. Eleven patients (31%) with leukemia died, whereas 21 patients (6%) in all other cancer groups combined died (\( p < 0.0001 \); Table 2). The leukemia group had a higher rate of discard secondary to death than all other cancer groups (24% versus 6%). The mean age of death for the leukemia group was 25.9 ± 7.5 years, and the median number of days banked until death was 336 (69–1037). All other disposition categories, including ongoing storage (43%), electively discarded

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**Outcomes for the 423 cancer patients who attempted banking**

- Ongoing storage (n=181)
- Electively discarded (n=129)
- Failed to bank a sample (n=45)
- Shipped or used for fertility treatments (n=36)
- Discarded due to death (n=32)

**Outcome for the 348 infertility patients who attempted banking**

- Ongoing storage (n=82)
- Electively discarded (n=138)
- Failed to bank a sample (n=20)
- Shipped or used for fertility treatments (n=108)
- Discarded due to death (n=0)

![Fig. 2. Sperm banking outcomes.](image-url)
(30%), failure to bank (11%), and shipped or used (9%), were similar between the various cancer groups (Fig. 2).

### 3.4. Comparison to infertility patients

Lastly, we compared our cancer cohort to patients banking for infertility reasons (Table 3). The cancer cohort was younger, less likely to be married, and had higher rates of failing to bank, owing to a significantly higher rate of azoospermia, than the infertility group. The overall semen parameters of median pre- and post-thaw sperm counts and motility were similar, however, and there was no difference between the groups in the ability to produce a sample (Table 3). Finally, compared to the infertility group, cancer patients banked samples longer, were more likely to continue ongoing storage, and were less likely to use samples (Fig. 2).

### 4. Comment

Our study extends the work of others [9,10] demonstrating that male cancer patients in the U.S. use sperm banking for fertility preservation. Additionally, we provide strong evidence that cancer patients can bank sperm nearly as effectively as men banking for infertility reasons. To our knowledge, this is the first report demonstrating that pre- and post-thaw sperm parameters are similar between the two groups. Our finding that cancer patients bank for longer than do men banking for infertility strongly supports the idea that sperm banking is a highly valued service offered to cancer patients.

Our data support the conclusions of earlier studies in several ways. First, other studies report that 4–16% of cancer patients used their banked sperm for fertility treatment. In the two studies from the U.S., the rates were 5% [10] and 8.4% [9] over 10 and 8 years, respectively. Over the course of 20 years, 9.5% of the patients used their samples in our facility or shipped them to another facility for use. Second, we observed approximately two-fold losses in sperm count and motility following storage in liquid nitrogen, similar to earlier studies [16–19]. Third, as seen in other studies [9,10], the frequencies of cancers in our study corresponded to the levels seen in reproductive-age men in the U.S. [1]. Fourth, our observed 5% rate of azoospermia was similar to the 1.1% to 13.9% rates seen in prior studies [17–20]. Fifth, as in the study by Menon et al. (in which only 3 of 156 patients aged 13–20 years old failed to produce a sample) age was not a significant factor in ability to produce a sample by masturbation: all 73 adolescents (≤21 year of age) in our study were able to do so. We emphasize this because some physicians are hesitant to offer sperm banking to adolescents for fear they will not be able to produce a sample. Finally, the most frequent outcome in our study was continued storage. At the end of our study, 181 cancer patients (48%) were continuing storage of their samples. Ongoing storage was also the most frequent outcome reported by Chung et al. (77%) and Kelleher et al. (52%).

We note two key differences between our findings and those of prior studies. First, although testicular cancer patients were reported to have the lowest median pre-thaw counts and motility in prior studies [10,16,17,19–22], in this study these parameters were lowest in leukemia patients. Some studies suggest that cancer patients have an intrinsic suppression of spermatogenesis, but the exact mechanism for suppression in leukemia patients is not clearly established [16,23–25]. Second, our observed mortality rate (7.6%) is lower than those from similar studies published in the past 5 years, which range from 12.0% to 20.3% [17,20,22]. The lower
rate may be due to improvements in cancer treatment or selection bias of patients referred for banking.

Improvements in cancer treatment and life expectancy lead patients to consider post-treatment quality of life. Because male-factor infertility is one of the most devastating long-term effects of anticancer treatment [26] and because sperm cryopreservation before gonadotoxic treatment is the only reliable method to preserve male fertility, numerous studies have recommended that sperm banking should be offered as a standard of care to all males who will have gonadotoxic therapy [27–29], especially given its low cost relative to other infertility treatment options. The median cost of banking in the U.S. is $358 with a median annual maintenance fee of $244 [30].

One obstacle to sperm banking is inadequate communication between physician and patient about cancer severity and risk of post-treatment infertility [31]. Given that informed consent must be obtained before providing chemotherapy or radiation, providers should be aware of and discuss potential effects of these agents on the gonads. Although cost does not seem to be a barrier to the majority of men who opt out of banking, it is a barrier for oncologists to begin the discussion [29,32]. Recent studies note that providers who care for cancer patients need to be better educated about the fertility preservation options that exist [33], especially as this lack of knowledge may create a communication gap [32]. Having standardized approaches in place to discuss future fertility and fertility preservation options can dramatically increase the proportion of patients who use these services [9,34,35].

Limitations of our study include the biases inherent in all retrospective studies. Another limit is the inability to quantify poor quality for the 12 patients who failed to bank for this reason. Lastly, we did not include the reason patients electively discarded. In our facility, a patient is not required to give a reason for discarding a sample, leaving those data incomplete.

The most significant strength of our study is the comparison of cancer patients to the infertile patients who banked at our institution. Other strengths of our study include its duration and sample size; it is the largest study to date from the U.S. reporting data on the usage, discard, ongoing storage, and mortality rates for cancer patients after semen cryopreservation.

In conclusion, our study supports earlier studies in providing evidence that sperm banking is a utilized modality of fertility preservation in patients with a myriad of cancer diagnoses in the U.S. We encourage oncologists to discuss sperm banking with all male cancer patients, regardless of prognosis, as the best means to preserve future fertility.

Acknowledgments

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