FERTILITY AND STERILITY®
VOL. 82, NO. 2, AUGUST 2004

Published by Elsevier Inc.
Printed on acid-free paper in U.S.A.

Normal semen parameters in cancer patients presenting for cryopreservation before gonadotoxic therapy

Similar sperm qualities in men with and without cancer were found. Patient and physician awareness and early referral for sperm banking are essential in preserving fertility potential in men with malignancies. (Fertil Steril® 2004;82:505–6. ©2004 by American Society for Reproductive Medicine.)

Prior investigators have reported that more than half of the men of reproductive age with malignancies, such as testicular cancer and lymphoma, have impaired semen quality (1, 2). Chemotherapy or radiotherapy can further damage spermatogenesis, with lasting effects of up to 5 years (3). With increased awareness of the need for sperm banking, men have been presenting for cryopreservation soon after diagnosis. However, physicians might fail to offer cryopreservation to men with cancer, assuming that the semen quality is too impaired and that the fertility potential will further be decreased by the process of cryopreservation (4). With sophisticated assisted reproductive techniques, pregnancies and deliveries have been reported with cryopreserved spermatozoa from cancer patients, without increased risk of congenital anomalies (5, 6). In addition, with excellent cure rates for testicular cancer and increased survival in many urologic and nonurologic malignancies, most cancer survivors want to have children. We present a comparative analysis of sperm quality and postthaw survival in men with and without malignancies.

The statistical database of all men seeking sperm cryopreservation at a single licensed and accredited sperm bank was reviewed from 1997 to 2001. Two hundred fourteen men with cancer and 22 men without cancer were evaluated. Two patients with azoospermia were excluded. One of these patients had azoospermia after a unilateral orchiectomy for seminoma, whereas the other had acute myelogenous leukemia. All specimens were collected by masturbation into a sterile container before the initiation of cancer treatment. A single technician performed semen analysis within 1 hour of collection. The parameters compared were patients' age, sperm volume, concentration, total count, motility, motile fraction, postthaw motility, and viability. Postthaw parameters were obtained after specimens were frozen for 24 hours and then thawed. All cancer patients, cancer patients with a total sperm count of 5×10^6 or greater, and those with acute leukemia were compared with men without cancer. Mann-Whitney rank sum test and *t*-test were used for data analysis. This study was issued a waiver of authorization by the North Shore-Long Island Jewish Health System institutional review board.

Of the cancer patients, 22.6% had nonseminomatous primary testicular cancer, 20.8% had Hodgkin's lymphoma, 18.8% had testicular seminoma, 12.3% had non-Hodgkin's lymphoma, 5.2% had prostate cancer, 4.3% had acute leukemia, and 16.0% had other types of cancer. Of the 22 men without cancer, 36.4% requested cryopreservation before vasectomy, and the remainder sought cryopreservation for other benign conditions. The mean age of men without cancer was 35.23 years (range, 19–55 years), and for cancer patients the mean age was 30.10 years (range, 14–67 years). Patients' age was the only statistically significant difference between any of the cancer groups compared with men without cancer ($P<.05$). None of the prefreeze or postthaw semen parameters were significantly different between patients with cancer compared with those without malignancies (Table 1).

Cryopreservation is often the only chance for fertility in men diagnosed with cancer who need urgent cancer treatments. Initially, the treatment of malignancy is the primary goal, but surviving men do not have to suffer the agony and disappointment of infertility that follow such therapy. Return of spermatogenesis after radiotherapy depends on the radiation dose. At doses of >400 cGy, 5 years or more is needed for spermatogenesis to resume and 9–18 months if <100 cGy is administered (7). Up to 25% of men might remain permanently infertile after infradiaphragmatic radiotherapy (8). The majority of men treated with commonly used platinum-based chemotherapeutic agents develop azoospermia that can last up to 4 years (9). Permanent sterility has been reported in almost all men with Hodgkin's lymphoma treated with COPP (cyclophosphamide, vincristine, procarbazine, prednisone) (10), with return of spermatogenesis in 50% of those treated with other agents, such as cisplatin.

As mentioned earlier, multiple studies have shown the inferior sperm quality of some cancer patients, such as those with testicular cancer and lymphoma. Hallak et al. (11) demonstrated that the motile sperm count of

Received April 15, 2003; revised and accepted December 11, 2003.
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0015-0282/04/$30.00
doi:10.1016/j.fertnstert.2003.12.045

TABLE 1

Comparison of prefreeze and postthaw semen analysis of men with and without cancer.

Group (no.)	Volume (mL)	Concentration ($\times 10^6$/mL)	Total count ($\times 10^6$)	Motility (%)	Motile fraction ($\times 10^6$)	Postthaw motility (%)	Postthaw viability (%)	Age (y)
No cancer (22)	2.83	67.1	199.96	48.36	101.41	76.40	78.03	35.23
All cancers (212)	2.32	61.07	157.94	46.79	81.60	68.76	73.33	30.10
	P>.1	*P*>.2	*P*>.1	*P*>.9	*P*>.1	*P*>.07	*P*>.2	*P*<.05
All cancers $>5 \times 10^6$ (192)	2.43	67.17	174.16	49.77	90.03	72.35	76.05	30.34
	P>.2	*P*>.6	*P*>.4	*P*>.5	*P*>.4	*P*>.1	*P*>.4	*P*<.05
Acute leukemia (9)	2.31	76.29	261.96	35.67	149.97	60.18	62.26	24.78
	P>.3	*P*>.6	*P*>.8	*P*>.2	*P*>.5	*P*>.1	*P*>.1	*P*<.05

Note: All *P* values are compared with men without cancer.

Rofeim. Normal semen parameters in cancer patients. Fertil Steril 2004.

patients with testicular cancer was lower prefreeze and postthaw compared with normal donors. In another study, the percent change in motility was greater after thawing for cancer patients compared with normal donors, although not statistically significant (12). However, other studies have not demonstrated a significant decline in sperm quality of cancer patients after cryopreservation compared with normal donors (13, 14). In our study, the semen quality of patients with cancer did not differ significantly from that of men without cancer. This change from prior investigations might be related to more rapid diagnosis and referral for sperm banking in cancer patients. Although a recent survey showed that 91% of oncologists agree that cryopreservation should be offered to all eligible men, only 10% always offered it, and 27% offered it only half the time (15). Lack of discussion time, presumed high cost, and unavailability of adequate facilities were reported as the most common reasons that sperm banking was not suggested. Another survey by the same investigators revealed that only 51% of eligible men diagnosed with cancer remembered being offered to bank sperm, and only 24% cryopreserved their semen (16).

We suggest that cryopreservation should be offered to patients diagnosed with cancer as soon as possible and before initiation of any therapy, such as orchiectomy. Petersen et al. (17) demonstrated that semen quality significantly decreases after orchiectomy for testicular cancer. Hospitalized men who present critically ill and need urgent chemotherapy, such as those with acute leukemia, should also be encouraged to cryopreserve sperm before beginning gonadotoxic therapy. Misconceptions and inaccurate information regarding infertility and sperm banking in men with cancer can lead to permanent impairment of fertility. The importance of educating health care professionals and counseling patients before surgical intervention or the start of gonadotoxic therapy cannot be overemphasized.

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References

1. Carrol PR, Whitmore WF, Herr HW, Morse MJ, Sogani PC, Bajorunas D, et al. Endocrine and exocrine profiles of men with testicular tumors before orchiectomy. J Urol 1987;137:420–3.
2. Nijman JM, Schraffordt Koops H, Kremer J, Sleijfer DT. Gonadal function after surgery and chemotherapy in men with stage II and III nonseminomatous testicular tumors. J Clin Oncol 1987;5:651–6.
3. Rustin GJS, Pektasides D, Bagshawe KD, Newlands ES, Begent RHJ. Fertility after chemotherapy for male and female germ cell tumors. Int J Androl 1987;10:389–92.
4. Kolodziej FB, Katzorke T, Propping D. Cryopreservation of human spermatozoa—evaluation of 93 semen depots. Andrologia 1990;22: 164–70.
5. Hallak J, Hendin BN, Thomas AJ Jr, Agarwal A. Investigation of fertilizing capacity of cryopreserved spermatozoa from patients with cancer. J Urol 1998;159:1217–20.
6. Lass A, Akagbosu F, Abusheikha N, Hassouneh M, Blayney M, Avery S, et al. A programme of semen cryopreservation for patients with malignant disease in a tertiary infertility center: lessons from 8 years' experience. Hum Reprod 1998;13:3256–61.
7. Rowley MJ, Leach DR, Warner GA, Heller CG. Effect of graded doses of ionizing radiation on the human testis. Radiat Res 1974;59:665–78.
8. Fossa SD, Aass N, Kaalhus O. Long-term morbidity after infradiaphragmatic radiotherapy in young men with testicular cancer. Cancer 1989;64:404–8.
9. Ohl DA, Sonksen J. What are the chances of infertility and should sperm be banked? Semin Urol Oncol 1996;14:36–44.
10. Kreuser ED, Xiros N, Hetzel WD, Heimpel H. Reproductive and endocrine gonadal capacity in patients treated with COPP chemotherapy for Hodgkin's disease. J Cancer Res Clin Oncol 1987;113:260–6.
11. Hallak J, Kolletis PN, Sekhon VS, Thomas AJ Jr, Agarwal A. Sperm cryopreservation in patients with testicular cancer. Urol 1999;54: 894–9.
12. Hallak J, Mahran A, Chae J, Agarwal A. Poor semen quality from patients with malignancies does not rule out sperm banking. Urol Res 2000;28:281–4.
13. Agarwal A. Semen banking in patients with cancer: 20-year experience. Int J Androl 2000;23(Suppl 2):16–9.
14. Agarwal A, Tolentino MV Jr, Sidhu RS, Ayzman I, Lee JC, Thomas AJ Jr, et al. Effect of cryopreservation on semen quality in patients with testicular cancer. Urol 1995;46:382–9.
15. Schover LR, Brey K, Lichtin A, Lipshultz LI, Jeha S. Oncologists' attitudes and practice regarding banking sperm before cancer treatment. J Clin Oncol 2002;20:1890–7.
16. Schover LR, Brey K, Lichtin A, Lipshultz LI, Jeha S. Knowledge and experience regarding cancer, infertility, and sperm banking in younger male survivors. J Clin Oncol 2002;20:1880–9.
17. Peterson PM, Skakkebaek NE, Rorth M, Giwercman A. Semen quality and reproductive hormones before and after orchiectomy in men with testicular cancer. J Urol 1999;161:822–6.