Semen cryopreservation for men banking for oligospermia, cancers, and other pathologies: prediction of post-thaw outcome using basal semen quality

Selene Degl'Innocenti, M.L.T.,[a] Erminio Filimberti, Ph.D.,[a] Angela Magini, M.D.,[a] Csilla Krausz, M.D.,[a] Giuseppe Lombardi, M.D.,[b] Maria Grazia Fino, M.L.T.,[a] Giulia Rastrelli, M.D.,[a] Mario Maggi, M.D.,[a] and Elisabetta Baldi, Ph.D.[a]

[a] Department of Biomedical Experimental and Clinical Science, Sexual Medicine and Andrology Unit, University of Florence and Azienda Ospedaliera; and [b] Spinal Unit, Azienda Ospedaliera-Universitaria Careggi, Florence, Italy

Objective: To evaluate post-thawing sperm parameters in a large series of men cryopreserving for different cancers and oligospermia.
Design: Retrospective observational study.
Setting: Semen cryopreservation laboratory.
Patient(s): Six hundred twenty-three patients undergoing semen cryopreservation for cancer or oligospermia who discontinued banking.
Intervention(s): None.
Main Outcome Measure(s): Postcryopreservation sperm motility and viability.
Result(s): In oligospermic men, recovery of motile sperm after cryopreservation was possible in only a few out of the 219 samples cryopreserved for this problem. Similarly, independent of the reason for which cryopreservation was required, if one basal semen parameter fell below the 5th percentile of the World Health Organization reference values, recovery of motile and viable spermatozoa after thawing was low. Among samples cryopreserved for cancer, those with testicular cancer showed the lowest basal semen quality and recovery after thawing. In cases of hematological cancers or other types of cancers, motility recovery was similar to that of non-cancer-related samples. Receiver operating characteristic analyses demonstrate that basal progressive and total motility predict the recovery rate of motile sperm after thawing with high accuracy, sensibility and specificity.
Conclusion(s): Our study demonstrates the ability of prefreeze semen parameters to predict cryosurvival in terms of sensitivity and precision. Using this information, the clinician could perform appropriate counseling about the future possibilities of fertility for the patient. (Fertil Steril® 2013;100:1555–63. ©2013 by American Society for Reproductive Medicine.)
Key Words: Sperm cryopreservation, sperm motility, oligospermia, cancer, sperm viability

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/deglinnocentis-semen-cryopreservation-oligozoospermia-cancer/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

Cryopreservation of spermatozoa is, at present, the most valuable and used way to preserve reproductive function in men undergoing gonadotoxic treatments such as chemo- or radiotherapies. In addition, sperm cryopreservation is increasingly used in case of other disorders, such as autoimmune diseases and myelodysplastic syndromes requiring treatments that may affect reproductive functions. Moreover, sperm cryopreservation is offered to patients with severe oligospermia (or even cryptozoospermia) or ejaculatory disorders with the intent of using cryopreserved sperm in case no sperm are found in the ejaculates on the day of intracytoplasmic sperm

Received May 29, 2013; revised July 30, 2013; accepted August 6, 2013; published online September 11, 2013.
S.D.I. has nothing to disclose. E.F. has nothing to disclose. A.M. has nothing to disclose. C.K. has nothing to disclose. G.L. has nothing to disclose. M.G.F. has nothing to disclose. G.R. has nothing to disclose. M.M. has nothing to disclose. E.B. has nothing to disclose.
Reprint requests: Mario Maggi, M.D., Dipartimento di Scienze Biomediche Sperimentali e Cliniche, Sezione di Fisiopatologia, Clinica, Università di Firenze, viale Pieraccini 6, I-50139 Firenze, Italy (E-mail: mario.maggi@unifi.it).

Fertility and Sterility® Vol. 100, No. 6, December 2013 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2013.08.005

injection (ICSI) (1) to have sperm available in the event of a decline in sperm count, which may occur in these patients (2).

Cryopreservation of spermatozoa was introduced in the early 1960s and is performed with different procedures. In the last version of the World Health Organization (WHO) manual for semen analysis, a protocol is indicated, but the procedure is not standardized (3). The consequences of cryopreservation on sperm functions are well-known. Spermatozoa may be heavily damaged by freezing-thawing procedures and total motility, viability, and morphology are severely affected in most samples (4–7). However, whether the different types of pathology requiring sperm cryopreservation may result in a different outcome of sperm quality at thawing has been studied only for cancer patients, and results are often controversial (8–14). For instance, when results of semen cryopreservation from testicular cancer patients were compared with those of donors, Said et al. (11) and Hotaling et al. (13) found lower cryosurvival rates, whereas Hallak et al. (9) did not find relevant differences. Similarly, whereas Hallak et al. (10) found lower post-thaw motility recovery in Hodgkin's lymphoma patients with respect to healthy donors, motility reduction in the former category of patients was similar to that of healthy donors in the study by Hotaling et al. (13). Outcome of cryopreservation in cases of severe oligospermia has not been evaluated so far. In addition, whether the expected decrease in sperm functions is related, or can be predicted, on the basis of semen quality on the day of cryopreservation has also been poorly documented. One study (15) reported that Kruger strict morphology assessment, among the conventional semen parameters, was the best predictor of progressive motility recovery after thawing in a small number of normozoospermic samples. Other studies (16, 17) evaluating the relationship between prefreezing and post-thawing semen characteristics demonstrated that higher concentration and prefreeze motility and fewer abstinence days are associated with an increased recovery rate in donors for a sperm bank. In general, it appears that, for normospermic samples, postcryopreservation recovery is related to basal semen quality; however, sensitivity and specificity of basal semen parameters in predicting cryosurvival rates have not been established.

Cryopreserved semen is used in assisted reproductive techniques (ART) and, in case of low motility recovery, ICSI is mandatory. Although most studies comparing ICSI using fresh or thawed spermatozoa do not reveal differences in reproductive outcome (18, 19), it appears that ICSI performed with motile spermatozoa gives better results with respect to immotile ones (20, 21). As a matter of fact, ICSI performed using cryopreserved spermatozoa from patients with different types of cancer or pathologies gives rise to variable clinical pregnancy and live-birth rates (12, 22). Owing to the detrimental effects of cryopreservation, the chance of finding motile sperm after thawing to perform the ICSI procedure is greatly decreased. Such a chance may decrease even more in pathological conditions (like testicular cancer and oligospermia) associated with detrimental effects on semen quality (11, 23–25). In light of these considerations, prediction of cryopreservation outcome on the basis of basal semen quality and type of pathology for which cryopreservation is required may help in the management and counseling of these patients.

The present study evaluated sperm motility and viability recovery rates after thawing and the relationship with precryopreservation semen quality in 822 semen samples from men affected by different types of neoplasia, oligospermia, or other pathologies requiring cryopreservation who discontinued sperm banking. Receiver operating characteristic (ROC) curves were used to identify the accuracy of the different semen parameters in predicting motility recovery rates. Our results demonstrate that the recovery rate of sperm motility and viability varies among the different pathologies. In addition, we show that precryopreservation sperm motility predicts motility recovery with a high accuracy.

MATERIALS AND METHODS

Patients

The study was conducted in semen collected from 623 patients undergoing semen cryopreservation in the Laboratory of Andrology of the Azienda Ospedaliera-Universitaria of Florence from 1998 to 2010 who discontinued sperm banking. A total of 822 semen samples have been collected from these subjects, as some patients underwent more than one semen collection to increase the number of cryopreserved straws. Of the 822 samples, 183 were cryopreserved because of hematological malignancies (122 for Hodgkin's lymphoma, 31 for non–Hodgkin's lymphoma, 27 for leukemia), 158 for testicular cancer (78 seminoma, 16 nonseminomatous germ cell tumors, 64 unknown), 83 for mixed cancer pathologies (15 urinary tract, 26 skeletal-muscle, 17 cerebral, 7 gastrointestinal, and 18 other types of cancer), 239 for oligospermia, 56 for ejaculatory disorders, 42 for other pathologies (mostly multiple sclerosis and autoimmune pathologies), and 61 for spinal cord injury (37 using electroejaculation and 24 with vibratory stimulation). All cancer patients cryopreserved sperm before initiation of the antineoplastic treatment. In case of testicular cancer, the majority of patients underwent cryopreservation after orchiectomy. Semen samples cryopreserved with baseline 0% viability ($n = 34$), although cryobanked for ethical reasons, were not considered in the statistical analysis.

All the data provided were collected as part of the routine clinical procedure, and therefore, according to the Italian law, approval from the local Ethics Committee was not required. In addition, informed consent had been obtained from all patients to use discarded, cryopreserverd sperm for research purposes.

Semen Samples for Cryopreservation

Semen samples were collected the same day of cryopreservation by masturbation in the laboratory. In exceptional cases, semen collection was performed at home. With the exception of spinal cord injury patients, all subjects were asked to observe 2–7 days of sexual abstinence. After semen analysis (see below), semen samples were frozen in liquid nitrogen tanks by a manually controlled freezing procedure according to Gandini et al. (26) with minimal modifications. Briefly,