Reproductive BioMedicine Online (2016) 33, 29–38

www.sciencedirect.com
www.rbmonline.com

REVIEW

Sperm cryopreservation and reproductive outcome in male cancer patients: a systematic review

Stefania Ferrari [a], Alessio Paffoni [a,*], Francesca Filippi [a], Andrea Busnelli [a,b], Walter Vegetti [a], Edgardo Somigliana [a]

[a] *Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Infertility Unit, via M. Fanti 6, 20122 Milan, Italy;*
[b] *Università degli Studi di Milan, Obstetrics and Gynecology, via Commenda 10, 20122 Milan, Italy*
* Corresponding author. *E-mail address:* alessio.paffoni@policlinico.mi.it (A Paffoni).

Stefania Ferrari received her degree in Biotechnology in 2007 and is now completing her residency in Medical Genetics at the University of Milan, Italy. She has been involved in fertility preservation and pre-implantation diagnosis programmes at the Infertility Unit of the Fondazione Ospedale Maggiore Policlinico in Milan.

Abstract This systematic review of the literature reports on the use and effectiveness of sperm banking programmes for cancer patients. Thirty studies with 11798 patients were included. The aggregated rate of use of cryopreserved semen was 8% (95% CI 8 to 9%). A statistically significant correlation emerged between the mean and median duration of follow-up and the rate of use (R^2 = 0.46; P = 0.03). The rate of patients discarding their frozen sample was reported in 11 studies. The aggregated rate was 16% (95% CI 15 to 17%). The rate of patients who used their frozen semen and achieved parenthood was reported in 19 papers. The aggregated rate was 49% (95% CI 44 to 53%). The rate of patients achieving parenthood with the use of frozen sperm is low and, from an economical perspective, the effectiveness of programmes of sperm banking might therefore be questioned. On the other hand, the low rate of patients discarding their frozen samples and the correlation between rate of use and duration of follow-up suggest that the calculated 8% rate of use may be an under-estimation and that cumulative rate of use may be substantially higher. Specific studies are, however, required to clarify this issue.

KEYWORDS: assisted reproductive techniques, cancer, cryopreservation, fertility preservation, semen preservation, sperm banks

http://dx.doi.org/10.1016/j.rbmo.2016.04.002
1472-6483/

Introduction

In the past few decades, therapeutic advances have improved the long-term survival of patients with cancer. Cancer treatments are frequently aggressive and unwanted side-effects are common, including threats to fertility. In men, several treatments can adversely affect spermatogenesis because the male gonads are highly susceptible to the toxic effects of chemotherapeutic agents or localized radiotherapy. Moreover, specific surgical approaches, such as retroperitoneal lymphadenectomy, may impair normal ejaculation (Tournaye et al., 2014).

Therapeutic agents have varying degrees of effects on gametogenesis, depending on sperm quality before treatment, type of malignancy (Botchan et al., 2013), drug characteristics, treatment regimen and patient susceptibility. Hence, it is not possible to predict reliably whether an individual patient will become permanently azoospermic or, conversely, whether he will resume partial to normal spermatogenesis after treatment (Meirow and Schenker, 1995; Meseguer et al., 2006; Revel et al., 2005; Tomlinson et al., 2015). For this reason, the Ethics Committee of American Society for Reproductive Medicine (2013) and the American Society of Clinical Oncology (Loren et al., 2013) have recognized the importance of consistently addressing the issue of fertility preservation in the course of cancer diagnosis and treatment in men. Both societies recommend clinicians to discuss with patients the potential effect of cancer treatments on fertility and to present options for fertility preservation (García et al., 2015). This is even more important for young cancer patients who have not yet started or completed their families (Chung et al., 2013; García et al., 2015). In the USA, up to 9.2% of patients diagnosed with cancer are younger than 45 years old, and up to 1.1% of male cancer patients are younger than 20 years (Siegel et al., 2014). Young patients and their families consider the threat of infertility as a major concern among cancer sequelae (Schover, 2009) and, for many patients, the knowledge that their fertility potential can be secured through sperm cryopreservation helps in the emotional battle against cancer (Saito et al., 2005).

Currently, the only way to efficiently preserve the reproductive potential in adult or adolescent male cancer patients remains sperm cryopreservation and its subsequent use in various assisted reproduction techniques if needed (Botchan et al., 2013; Tournaye et al., 2014). Sperm cryopreservation represents a simple and effective way of preserving fertility potential even in cancer patients with poor semen characteristics (Chung et al., 2013). It has been reported that, after cryopreservation, only a few patients actually use their frozen sperm for assisted reproduction techniques, and only a subgroup of them achieve parenthood; this figure has been relatively unaffected over the last decades despite the development and increasing availability of modern IVF treatments (Fosså et al., 1989; van Casteren et al., 2008). The utilization rate of cryopreserved semen is often less than 10–15% and differs widely between studies as recently summarized by van Casteren et al. (2008). In particular, a mean percentage of use of 7% (range 4–16%) and a rate of couples achieving parenthood of 45% (range 33–72%) have been reported, suggesting that less than 4% (0.45×0.07) of affected men actually benefit from sperm cryostorage (van Casteren et al., 2008).

From a public health perspective, the cost-effectiveness of sperm banking programmes for cancer patients may be questioned. Rational decisions in the allocation of financial resources is now a priority in all areas of medicine, and fertility preservation cannot escape this rule (ESHRE Capri Workshop Group, 2015; Hall et al., 2016).

On the other hand, conclusions emerging from the analysis of available results up to now may be premature. Sperm banking is a long-term programme requiring long-term data before definite conclusions can be drawn. It is plausible that a consistent proportion of men who did not use their sample at the time of the analysis will do it in the future (Ragni et al., 2003). In this litereature review, we intend to update the current evidence for male oncofertility with the inclusion of recent contributions and particular emphasis on the potential confounding effect of the duration of follow-up. We therefore carried out a systematic review of the literature on the use and effectiveness of sperm banking programmes for cancer patients focusing on two main outcomes: the usage rate of cryopreserved semen; and the following success rate in terms of pregnancies and live births obtained with the use of spermatozoa frozen before cancer treatment.

Materials and methods

This review was restricted to published research articles that reported on the usage rate of cryopreserved semen, on the success rate in terms of pregnancies and live births obtained, or both, with the use of spermatozoa frozen before cancer treatment. As published de-identified data were used, the present study was exempt from Institutional Review Board approval.

The literature was searched to identify pertinent studies published between January 2000 and July 2015. This time period was selected so that more recent usage rates could be examined. Since 2000, modern assisted reproduction techniques, such as intracytoplasmic sperm injection, have became more widely available, and more recent studies are reporting on longer follow-up. In particular, the electronic databases *PUBMED* and *SCOPUS* were searched using the following mixture of terms and keywords: (cryopreservation OR preservation OR banking OR cryostorage OR storage) AND (sperm OR semen) AND (cancer OR tumor OR malignancy OR neoplasm). Filters were applied for English language, type of paper (to exclude review papers), human species and male sex. After eliminating duplicates, the title of the papers were checked to exclude case reports, papers describing female or prepubertal cancer patients, exclusive use of surgical retrieval of spermatozoa, effects of treatments, the influence of physiological parameters, cellular biology, testicular tissue or stem cell preservation and post-mortem use of sperm. In addition, guidelines, recommendations, surveys of professionals and articles on ethical, legal and psychological issues were discarded. Abstracts were then read and the same parameters for selection were used. The reference lists of initially selected and pertinent articles were reviewed to identify further reports that could be included. Selected studies were fully read for final selection, and only the papers on the use rate of cryopreserved samples were included. Abstracts of scientific meetings and conference proceedings were not