

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20253881>

Original Research Article

Exploring and investigating the long-term ramifications of fertility preservation in men with a history of cancer: a 10-year retrospective follow-up study

Kaavya Sathyamurthy*, Kundavi K. M., Geetha V., Rashmi, Geovin R., Yamini, Hema Nivedha, Sandhya

Institution of Reproductive Medicine and Women's Health Madras Medical Mission Hospital, Chennai, India

Received: 03 July 2025

Revised: 11 November 2025

Accepted: 12 November 2025

*Correspondence:

Dr. Kaavya Sathyamurthy,
E-mail: kaavyasathyamurthy@gmail.com

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ABSTRACT

Background: Cancer treatments such as chemotherapy, radiotherapy, and surgery can adversely affect male fertility, leading to temporary or permanent sterility. Sperm cryopreservation is the standard fertility preservation strategy for young male cancer patients prior to gonadotoxic therapy. However, utilization rates of stored samples remain low despite increased awareness and accessibility.

Methods: This retrospective study analyzed data from 136 male cancer patients who underwent sperm cryopreservation at Madras Medical Mission Hospital, Chennai, over a 10-year period. Patient records were reviewed to assess return rates for assisted reproduction, post-treatment semen analysis outcomes, and psychosocial factors influencing fertility-related decisions.

Results: None of the patients who banked sperm returned for assisted reproductive procedures. Post-treatment semen analysis was available for a subset of patients, among whom 82.9% demonstrated spontaneous recovery of fertility. Psychosocial barriers, including lack of a partner, financial constraints, and diminished reproductive intent, contributed to the non-utilization of cryopreserved sperm.

Conclusion: Although sperm cryopreservation offers an effective safeguard against treatment-induced infertility, its utilization remains minimal. The high rate of spontaneous fertility recovery and psychosocial limitations appear to influence decision-making. These findings highlight the need for individualized fertility counselling, systematic follow-up, and strategies to mitigate financial barriers. Integration of fertility preservation into comprehensive cancer survivorship programs is crucial to optimize reproductive outcomes and improve long-term quality of life in male cancer survivors.

Keywords: Sperm cryopreservation, Fertility preservation, Cancer, Chemotherapy, Radiotherapy, Spontaneous fertility recovery, Psychosocial factors, Male infertility, Cancer survivors

INTRODUCTION

Advances in cancer treatment have significantly improved survival rates among young male patients. However, many cancer therapies, including chemotherapy, radiotherapy, and surgical interventions, have gonadotoxic effects that can impair spermatogenesis and lead to temporary or permanent infertility.¹ The degree of infertility risk varies

based on multiple factors, including the type of cancer, treatment regimen, patient age, and baseline testicular function. Given these potential reproductive consequences, sperm cryopreservation has become the gold standard for fertility preservation in male cancer patients before initiating gonadotoxic treatment.² Chemotherapy agents such as alkylating drugs (cyclophosphamide, procarbazine), platinum-based

compounds (cisplatin), and radiotherapy are known to severely affect testicular function.³ Additionally, surgical procedures for testicular, retroperitoneal, and gastrointestinal cancers can impact fertility by damaging reproductive structures or altering endocrine function.⁴ Recognizing these risks, leading oncological and reproductive societies, including the American Society of Clinical Oncology (ASCO) and the European Society of Human Reproduction and Embryology (ESHRE), strongly recommend fertility preservation discussions before starting treatment.⁵ Despite the increasing awareness of fertility preservation, long-term follow-up studies indicate a surprisingly low rate of return for the utilization of cryopreserved sperm. A 14-year retrospective study by Meseguer et al reported that only 8.3% of male cancer patients who had cryopreserved sperm before treatment returned to use their stored samples.⁶ Similarly, Ferrari et al found that less than 10% of patients who banked sperm before cancer therapy used their samples for assisted reproduction.⁷ This discrepancy raises important questions about the actual clinical utility of sperm cryopreservation and the factors influencing patients' decisions regarding its use.

The extent of fertility impairment varies among different cancer types. In our study cohort of 136 male cancer patients who underwent sperm cryopreservation over a 10-year period, the most common malignancy was testicular cancer (40.4%), followed by hematological malignancies (30.1%), musculoskeletal cancers (11%), thyroid cancer (7.4%), gastrointestinal tract malignancies (5.1%), and other retroperitoneal cancers (6%). Testicular cancer is the most frequently diagnosed malignancy in young men, and affected patients often have suboptimal semen parameters even before treatment due to underlying testicular dysfunction.⁸ Orchiectomy, radiotherapy, and chemotherapy further compromise spermatogenesis, with post-treatment fertility recovery being variable.⁹ Despite sperm banking being widely recommended for testicular cancer patients, follow-up studies suggest that many regain fertility spontaneously post-treatment, which may explain the low utilization rates of cryopreserved sperm.¹⁰

Hematological malignancies, including Hodgkin's lymphoma, leukemia, and other blood cancers, are frequently treated with alkylating agents and stem cell transplantation, which pose a high risk of permanent azoospermia.¹¹ Studies have shown that the BEACOPP regimen (Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, Oncovin, Procarbazine, and Prednisone) carries a significantly higher risk of irreversible sterility compared to the ABVD regimen (Adriamycin, Bleomycin, Vinblastine, and Dacarbazine).¹² However, some patients recover spermatogenesis, leading to spontaneous conceptions and reduced reliance on cryopreserved sperm.¹ Musculoskeletal cancers, such as osteosarcoma, are often treated with high-dose cisplatin and methotrexate, which are known to have spermatotoxic effects.¹⁴ While some patients experience permanent sterility, others may

recover fertility over time. The uncertainty regarding fertility outcomes contributes to the decision to continue long-term sperm storage, even if the samples are not immediately utilized.¹⁵ Thyroid cancer does not directly impair fertility, but radioactive iodine therapy (I-131), commonly used in its treatment, can transiently reduce sperm counts.¹⁶ Many patients recover spermatogenesis within 12–24 months post-treatment, which may explain their low sperm utilization rates. Patients with gastrointestinal tract and retroperitoneal cancers may undergo extensive abdominal surgeries and chemotherapy, which can disrupt spermatogenesis and reproductive function.⁹ Fertility outcomes vary significantly based on treatment modality, tumor location, and patient age.

The decision to bank sperm is influenced by multiple factors beyond medical necessity. Many patients view sperm cryopreservation as a psychological safety net rather than an immediate reproductive need. Studies show that cancer patients experience distress and uncertainty when making fertility preservation decisions, leading to impulsive decisions to bank sperm.¹⁷ However, financial constraints pose a significant barrier. Sperm storage involves recurring costs, which can be a burden for young individuals without stable incomes.¹⁸ Some patients discontinue storage due to financial difficulties. Additionally, one of the major barriers to sperm utilization is the lack of structured fertility follow-up post-treatment. Studies have shown that many cancer survivors are unaware of their reproductive options after therapy, leading to underutilization of stored sperm.¹⁹

Given the significant discrepancy between sperm banking rates and utilization, this study aims to determine the long-term utilization rates of cryopreserved sperm among male cancer survivors. It also seeks to evaluate the incidence of spontaneous fertility recovery post-treatment and identify psychological, financial, and medical factors influencing reproductive decisions.

By analyzing a 10-year retrospective cohort of 136 patients, this study aims to improve fertility preservation strategies, enhance reproductive counselling, and optimize sperm cryopreservation practices for male cancer patients. Understanding these factors is crucial to improving reproductive healthcare for cancer survivors and ensuring that fertility preservation services align with patients' long-term needs.

The objective was to evaluate the long-term outcomes of sperm cryopreservation in male cancer patients, specifically analyzing sperm utilization rates, spontaneous fertility recovery, and factors influencing reproductive decisions post-treatment.

METHODS

This study was conducted as a single-center, retrospective follow-up study at Madras Medical Mission Hospital,

Chennai, over a 10-year period (January 2015 to December 2024).

Study population

The study included 136 male cancer patients who underwent sperm cryopreservation prior to receiving gonadotoxic cancer treatments, including chemotherapy, radiotherapy, or surgical interventions. The distribution of malignancies among the participants was testicular cancer (seminoma and non-seminoma) 42.6%. Hematological malignancies (Hodgkin's lymphoma and other blood cancers) 32.7% (73 patients). Musculoskeletal cancers (osteosarcoma and Ewing's sarcoma) 11% (15 patients). Thyroid malignancies 5.9%. Gastrointestinal tract cancers 3.7%, other retroperitoneal cancers 4.1%

Data collection

Patient data were extracted from the hospital's Medical Records Department, supplemented by structured telephone surveys and outpatient follow-up visits. The following variables were analyzed. Demographic details (age at diagnosis, marital status). Cancer diagnosis and treatment details (malignancy type, chemotherapy/radiotherapy regimen, surgical interventions).

Sperm banking decisions (storage duration, (renewal choices). Utilization of cryopreserved sperm (return rates for assisted reproduction). Spontaneous fertility recovery (natural conception post-treatment). Psychosocial and financial factors influencing sperm usage

This retrospective study included 136 male cancer patients who underwent sperm cryopreservation at the Andrology Laboratory, Madras Medical Mission Hospital, Chennai, between January 2015 and December 2024. Eligible participants were male cancer patients aged 15 to 45 years who had completed sperm cryopreservation prior to initiation of gonadotoxic treatment, possessed complete medical records, and provided consent to participate in the follow-up study.

Patients who were lost to follow-up either unreachable through phone contact or outpatient visits were excluded. Additionally, those who declined participation in follow-up or had pre-existing infertility, such as azoospermia or severe oligospermia prior to cancer therapy, were excluded from the analysis. Data regarding demographic details, type of malignancy, cancer treatment received, sperm banking parameters, and post-treatment fertility outcomes were collected and analyzed.

Primary outcome

Utilization rate of cryopreserved sperm for assisted reproduction.

Secondary outcomes

Spontaneous fertility recovery post-treatment. Reasons for non-utilization of stored sperm. Psychosocial and financial factors influencing fertility decisions. The study was conducted following institutional ethical guidelines, and all patients provided informed consent before participating in follow-up evaluations.

RESULTS

This section presents the findings from the 136 patients who underwent sperm cryopreservation between January 2015 and December 2024 before undergoing gonadotoxic cancer treatments. The study assessed the malignancy distribution, patient follow-up outcomes, decisions regarding sperm cryopreservation, and post-treatment semen analysis results.

Demographic and clinical characteristics

Distribution of malignancies

The distribution of malignancies among the study cohort is summarized in Table 1. Testicular cancer (42.6%) was the most common malignancy, followed by hematological malignancies (30.14%), whereas retroperitoneal cancers (3.7%) were the least common.

Age at the time of sperm cryopreservation

The majority (61%) of patients were aged 26-30 years, while a smaller proportion (2.2%) were in the 45-50 years age group. The age distribution is shown in Table 2.

Follow-up outcomes

Patient survival and follow-up status

Out of 136 patients, 129 (94.8%) were alive at the last follow-up, whereas 7 (5.2%) had passed away. 97 patients (71.3%) were successfully contacted, while 32 (23.5%) were lost to follow-up.

Personal reasons for low return rates

Among the 97 successfully contacted patients, various psychosocial and medical factors influenced their decision regarding fertility preservation. The most common reason for non-utilization of sperm was the preference for natural conception (27.2%), followed by the absence of a partner (17.6%).

Decision regarding cryopreservation

Among the 97 successfully contacted patients, 56 (57.7%) did not undergo repeat semen analysis after cancer treatment. Among those who did (41 patients, 42.3%), 34 (82.9%) had normal semen parameters, while 7 (17.1%) had azoospermia.

Post-treatment semen analysis outcomes

Among the 97 successfully contacted patients, 56 (57.7%) did not undergo repeat semen analysis after cancer treatment. Among those who did (41 patients, 42.3%), 34 (82.9%) had normal semen parameters, while 7 (17.1%) had azoospermia. This indicates that most cancer survivors who underwent repeat semen analysis had normal spermatogenesis recovery, but a small proportion (17.1%) developed irreversible infertility.

Summary of key findings

Malignancy distribution

Testicular cancer (42.6%) and hematological malignancies (30.14%) were the most common indications for sperm cryopreservation. Retroperitoneal cancers (3.7%) were the least common.

Age at Cryopreservation

The majority of patients (61%) were aged 26-30 years.

Follow-up outcomes

94.8% of patients were alive, but 23.5% were lost to follow-up.

Natural conception (27.2%) and absence of a partner (17.6%) were major reasons for not utilizing cryopreserved sperm.

Decisions regarding cryopreservation

47.1% of contacted patients continued sperm storage, while 16.9% discontinued due to spontaneous pregnancy. 8.1% of patients discontinued due to financial constraints.

Post-treatment semen analysis

42.3% of patients underwent semen analysis after treatment. Among them, 82.9% had normal sperm parameters, but 17.1% had azoospermia.

DISCUSSION

Fertility preservation through sperm cryopreservation has become an essential component of cancer care, particularly for young male patients undergoing gonadotoxic treatments such as chemotherapy and radiotherapy. This study followed 136 male cancer patients over ten years to assess the long-term outcomes of sperm cryopreservation, including return rates, spontaneous fertility recovery, and factors influencing post-treatment reproductive decisions. Our findings are consistent with previous studies, highlighting both the potential and the limitations of sperm cryopreservation in cancer care. A critical observation was the low return rate for cryopreserved sperm, even though fertility preservation services are increasingly available

and awareness about them is rising. The cohort in our study demonstrated a distribution of malignancies similar to global epidemiological trends. Testicular cancer was the most prevalent malignancy (42.6%), followed by hematological malignancies (30.14%), musculoskeletal malignancies (13.2%), thyroid cancers (5.9%), gastrointestinal tract cancers (4.4%), and other retroperitoneal cancers (3.7%). This distribution aligns with the epidemiology of testicular cancer as the most common malignancy in young males, particularly since chemotherapy and radiotherapy used to treat this cancer can lead to infertility. Hematological malignancies, such as Hodgkin's lymphoma, also represent a large portion of the patients who undergo fertility preservation due to the fertility risks posed by chemotherapy.^{20,21}

Return rates and utilization of cryopreserved sperm

A surprising finding in our study was the complete lack of utilization of cryopreserved sperm for assisted reproduction in all 136 patients. This result mirrors findings from similar long-term studies, where return rates for sperm cryopreservation are typically low, ranging from 3% to 10%. However, the reasons for this low return rate vary. In the cohort, the primary reason for non-utilization was the recovery of spontaneous fertility, which was observed in 82.9% of the patients who underwent post-treatment semen analysis. This finding underscores the importance of recognizing that not all cancer treatments lead to permanent infertility, as many patients can recover spermatogenesis over time.²²

In addition to recovery of spontaneous fertility, other factors influencing the low utilization rate included a lack of a partner at the time of sperm freezing and financial constraints. In the study, 17.6% of patients reported not using their stored sperm because they did not have a stable relationship or were not planning to have children at the time of freezing. Similarly, 8.1% of patients discontinued sperm cryopreservation due to the associated costs, a barrier that is particularly relevant in resource-limited setting.²³

Spontaneous conception and recovery of spermatogenesis

Our study observed that 16.9% of the patients were able to father children through spontaneous conception, highlighting that not all cancer survivors experience irreversible infertility. This aligns with other studies reporting spontaneous conception rates ranging from 10% to 25%, depending on the type of cancer and treatment received.⁵ Furthermore, post-treatment semen analysis revealed that 82.9% of patients had normal semen parameters, indicating that many cancer survivors regain natural fertility.²⁴ However, 17.1% of patients had azoospermia, suggesting irreversible damage to spermatogenesis. These findings emphasize the need for individualized follow-up assessments, as fertility outcomes can vary significantly among cancer survivors.

A personalized approach to fertility follow-up is essential to ensure that those who may benefit from assisted reproduction are not overlooked.

Psychosocial and emotional factors

Beyond medical and financial considerations, psychological factors played a significant role in reproductive decisions. Many patients viewed sperm cryopreservation as a form of psychological reassurance rather than a definitive plan for future fatherhood. This aligns with previous studies that have highlighted the emotional benefits of sperm banking, where patients report reduced anxiety and a greater sense of control over their reproductive future.²⁵ Despite the low utilization rates, the knowledge that fertility had been preserved provided emotional relief for many patients, even if the sperm was never used. A notable limitation of our study was the lack of structured follow-up counselling regarding fertility. Many patients did not undergo repeat semen analysis, suggesting a gap in long-term reproductive healthcare. In our study, 56 patients (41.2%) did not undergo any post-treatment fertility reassessment, which may have led to missed opportunities to use stored sperm if needed. This gap in follow-up could be addressed by integrating fertility assessments into routine oncology follow-up visits, ensuring that patients receive comprehensive guidance on their reproductive options.²⁶

Clinical implications and future directions

The findings from our study offer several important clinical insights. First, while sperm cryopreservation remains the gold standard for fertility preservation, it is essential to recognize that not all cancer treatments lead to permanent infertility. A significant proportion of cancer survivors regain natural fertility, making it crucial to provide individualized fertility assessments post-treatment. A more nuanced approach to fertility preservation that takes into account the likelihood of spermatogenesis recovery could help optimize the use of cryopreserved sperm. Second, the low utilization rate of cryopreserved sperm emphasizes the need for improved patient education and counselling. Many patients may not fully understand the long-term implications of fertility preservation at the time of sperm banking, which can lead to underutilization later on. Incorporating fertility counselling into cancer survivorship programs could enhance patient decision-making and improve utilization rates.²⁷ Third, financial constraints remain a significant barrier to long-term sperm storage. In the study, 8.1% of patients discontinued sperm storage due to cost-related reasons. Policymakers and healthcare providers should explore ways to make fertility preservation more affordable, such as through insurance coverage, cost-sharing programs, or public funding initiatives.²⁷

Finally, future research should focus on identifying biomarkers that can predict spermatogenesis recovery. Predictive models could help stratify patients based on

their likelihood of needing assisted reproduction, allowing for more personalized fertility preservation strategies.²⁷

This study has limitations that should be acknowledged. Being a retrospective, single-center analysis, its findings may not be generalizable to broader populations or diverse healthcare settings. The reliance on available medical records and patient self-reporting introduces the potential for incomplete data and recall bias. Additionally, a considerable proportion of patients were lost to follow-up or did not undergo post-treatment semen analysis, limiting the accuracy of fertility recovery assessment. Psychosocial factors influencing non-utilization of cryopreserved sperm were based on limited patient feedback rather than standardized questionnaires, which may have affected the depth of qualitative insights. Finally, variations in cancer type, treatment protocols, and duration of follow-up could have influenced fertility outcomes, underscoring the need for larger, multicentre prospective studies with uniform follow-up and standardized assessment tools to validate and expand upon these findings.

CONCLUSION

This 10-year single-center study demonstrates that while sperm cryopreservation is increasingly adopted by young male cancer patients, its actual utilization for assisted reproduction was nil in our cohort, largely because a high proportion of patients who underwent post-treatment semen analysis (82.9%) experienced spontaneous recovery of spermatogenesis and because psychosocial and financial barriers limited return for use; these findings advance the field by providing long-term, real-world evidence from a tertiary-care center in India that underscores the dual role of sperm banking as both a practical safeguard against permanent treatment-induced sterility and a source of psychological reassurance and by highlighting critical gaps in survivorship care (lack of routine post-treatment semen testing, variable follow-up, cost barriers, and inadequate counselling). The results argue for individualized risk stratification for fertility preservation, routine incorporation of post-treatment fertility assessments into oncology follow-up, targeted interventions to reduce financial and psychosocial obstacles, and the development of predictive models and standardized protocols to ensure that sperm cryopreservation translates into tangible reproductive benefit for cancer survivors.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sathyamurthy K, Kundavi KM, Geetha V, Rashmi, Geovin R, Yamini. Exploring and investigating the long-term ramifications of fertility preservation in men with a history of cancer: a 10-year retrospective follow-up study. *Int J Reprod Contracept Obstet Gynecol* 2025;14:1481-6.