

Male fertility preservation in oncology: patients' profile and clinical guidance importance

Preservação de fertilidade masculina em oncologia: perfil dos pacientes e importância da orientação clínica

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ABSTRACT

AIMS: To evaluate the profile of men with cancer who performed semen cryopreservation prior/during treatment and address the importance of this method for reproductive health.

METHODS: This was a transversal and retrospective study which used a database from a Reproductive Medicine Center located in Brazil. A total of 150 male patients who performed semen cryopreservation due to cancer diagnosis, from January 2014 to December 2017, were included.

RESULTS: The profile of men seeking fertility preservation prior/during treatment for cancer was young adults, single, childless, with higher education. Oncologists were the ones who reported more patients for semen cryopreservation followed by urologists and hematologists. With regards to tumor diagnosis frequency, testicular was the most diagnosed, followed by Hodgkin's/non-Hodgkin's lymphoma, leukemia, prostate and rectal tumor, along with retroperitoneal tumor.

CONCLUSION: Data brought the reflection on the cultural and financial barriers involved for the accomplishment of cryopreservation. Health professionals attending cancer patients should consider the importance of educational and incentive activities to prevent male fertility. Future research on the subject should be carried out.

KEYWORDS: Male fertility; fertility preservation; cryopreservation; neoplasms; reproductive age.

RESUMO:

OBJETIVO: Conhecer o perfil dos homens portadores de neoplasias malignas que preservaram sua fertilidade através da técnica de criopreservação de sêmen.

METODOLOGIA: A amostra foi composta por 150 pessoas do sexo masculino que realizaram a criopreservação de sêmen no período de janeiro de 2014 a dezembro de 2017. Trata-se de um estudo quantitativo, descritivo, transversal onde foram utilizados dados secundários de um banco de dados de um Centro de Medicina Reprodutiva situado em Porto Alegre, Rio Grande do Sul.

RESULTADOS: Os resultados demonstraram que o perfil dos homens com câncer que realizaram a criopreservação de sêmen é, em sua maioria, de jovens adultos, solteiros, sem filhos, que estão preocupados em manter sua capacidade reprodutiva após a terapêutica oncológica.

CONCLUSÃO: O conhecimento do perfil de pacientes que buscam a preservação dos gametas em casos de doenças oncológicas pode contribuir para o entendimento e possível sugestão de indicação pelos profissionais envolvidos neste tipo de abordagem.

DESCRITORES: Fertilidade masculina; preservação de fertilidade; criopreservação; neoplasias; idade reprodutiva.

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INTRODUCTION

According to The National Cancer Institute José de Alencar (in portuguese, *Instituto Nacional do Câncer*), 300,000 new male cancer cases were estimated in Brazil in 2018. Among them the most frequents are prostate, trachea, bronchus and lung, colorectal, stomach, oral cavity, esophagus, bladder, larynx and leucemia [1].-

The treatment of neoplasm consists of chemotherapy, radiotherapy, surgeries and bone marrow transplants, and there is often a need to perform the combined treatments for a good response. However, it is not possible to maintain a balance between fertility preservation and oncological therapy, or to predict whether these substances will temporarily or permanently affect reproductive capacity [2].

With regards to the fact that most patients affected with malignant neoplasms are in reproductive age and considering that they could manifest a desire for paternity, it has been verified the importance of health professionals to provide information on fertility preservation for reproductive health promotion [2]. In this context Oncofertility is becoming more common with the objective of improving the reproductive future of people who have had cancer. This interdisciplinary approach is being contemplated in many clinics worldwide [3].

Male fertility preservation could be achieved through sperm cryopreservation at subzero temperatures (-196°C in liquid nitrogen), which is a well-established technique. At -196°C, the biochemical reactions that lead to cell death are stopped [4].

According to European Association of Urology, semen cryopreservation should be offer to all man who are candidates for chemotherapy, radiation therapy, or surgical interventions that might interfere with spermatogenesis or cause ejaculatory disorders [4].

Based on a cohort study, 56.8% of 118 couples having intracytoplasmic sperm injection using pretreatment cryopreserved sperm achieve clinical pregnancy. In the same study, according to type of neoplasm, prostate cancer had worst semen parameters prior to treatment and achieve only 18.2% while testicular cancer performed 58% of clinical pregnancy rate [5].

For prepubertal minor children, the only fertility preservation options are testicular cryopreservation, which are still investigational [2].

The importance of preserving fertility in cases of cancer can be observed in clinical practice with the high number of patients who did not provide semen cryopreservation prior cancer treatment (for lack of

knowledge, sometimes), and look for sperm banks after treatment.

It is of great importance to understand the profile of patients who have sought to preserve fertility. Thus, the objective of this study was to evaluate the profile of men with cancer who performed semen cryopreservation prior to treatment and address the importance of this method for reproductive health.

METHODS

This was a transversal and retrospective study performed at a Reproductive Medicine Center, in Brazil. A total of 150 male patients who performed semen cryopreservation due to cancer diagnosis, from January 2014 to December 2017, were included. The database was created through clinical data records followed by a statistical analysis. The patient's profile was constructed according to sociodemographic variables (age, education, marital status, race, number of children) and diagnostic criteria (tumor type, time since diagnosis, medical specialty that referred to the infertility clinic, previous tumor surgery, and time of sperm collection before or after chemotherapy/radiotherapy).

The project was approved according to National Health Council Resolution 466/2012, by University of Vale do Rio dos Sinos Ethics Committee, number 1.874.712.

RESULTS

Initially, the percentage of patients who performed semen cryopreservation per year was analyzed. It was found that 34 (22.6%) semen samples were cryopreserved in 2014, 43 (28.6%) in 2015, 42 (28%) in 2016 and 31 (20.6%) in 2017 (**Figure 1**).

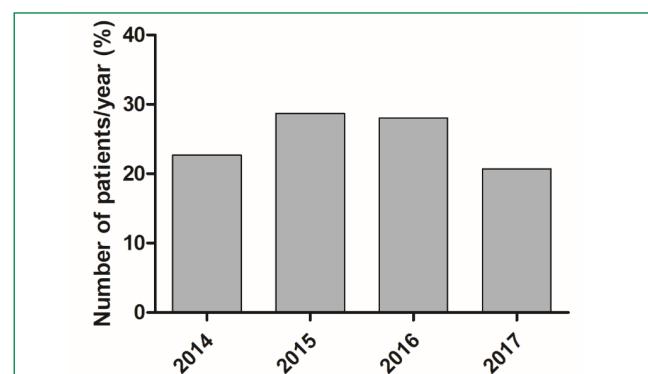


Figure 1. Percentage of patients who performed semen cryopreservation per year. Source: Data collected from the Reproductive Medicine Center database (2014-2017).

Sociodemographic Variables

The population mean age and standard deviation was 30.7 ± 8.6 years old, ranging from 14 to 59 years old. The **Figure 2** shows the frequency of patients per age who performed semen cryopreservation.

The complete profile of the population under study according to sociodemographic variables are shown in **Table 1**.

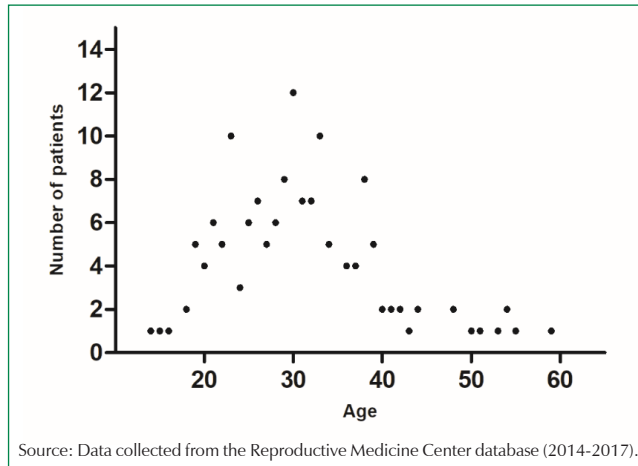


Figure 2. Number of patients who performed semen cryopreservation per age.

Table 1. Profile of the population under study according to sociodemographic variables.

Sociodemographic Variables	%
Caucasians	97.0
Marital status	
Married or In a Stable union	49.5
Not married	48.7
Separated	1.8
Education	
Elementary School/ Middle-school	3.4
High school	21.8
High school (incomplete)	2.5
Higher education	51.3
Higher education (incomplete)	21.0
No Children	80.7

Source: Data collected from the Reproductive Medicine Center database (2014-2017).

Diagnostic Criteria Variables

The study of diagnostic Criteria variables showed that oncologists were the ones who reported more patients for semen cryopreservation followed by urologists and hematologists. With regards to tumor diagnosis frequency, testicular was the most diagnosed in this cohort study, followed by Hodgkin's/non-

Hodgkin's lymphoma, leukemia, prostate and rectal tumor, along with retroperitoneal tumor.

It was observed that most patients took more than 30 days to do the first seminal collection, and 7.6% of patients had already started chemotherapy and/or radiotherapy prior to cryopreservation. The complete study data of diagnostic criteria variables are mentioned in **Table 2**.

The tumor types frequencies varied per year. Data are described in **Figure 3**.

Table 2. Profile of the population under study according to diagnostic criteria variables.

Diagnostic Criteria Variables	%
Specialty that referred to the infertility clinic	
Oncology	41.3
Urology	28.0
Hematology	9.3
Other specialties	13.2
Tumor Type frequencies	
Testicular tumor	57.3
Hodgkin's / Non-Hodgkin Lymphoma	15.3
Colorectal tumor	2.0
Prostate tumor	4.0
Leukemia	5.3
Retroperitoneal tumor	2.0
Other Tumors	14.0
Time since diagnosis, (days)*	
01-10	22.6
11-20	23.6
21-30	17.0
> 30	36.8
Previous treatment 139	
Surgery [†]	30.9
Surgery + chemotherapy / radiotherapy	2.9
Chemotherapy / radiotherapy	2.9
No previous treatment	63.3

* From tumor diagnosis to cryopreservation; [†] Partial or total tumor removal.

Source: Data collected from the Reproductive Medicine Center database (2014-2017).

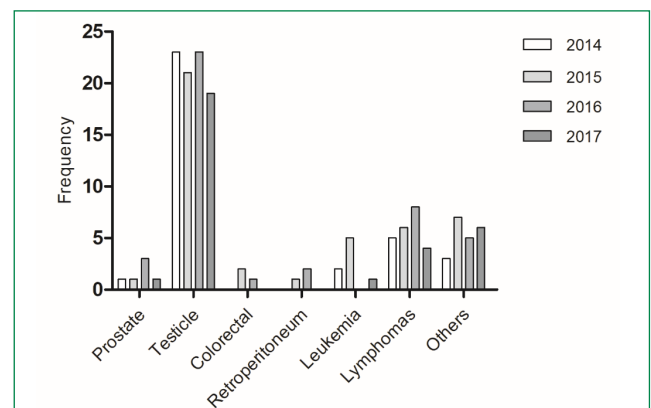


Figure 3. Tumors types frequencies (per year) of the population under study (n=150) Source: Data collected from the Reproductive Medicine Center database (2014-2017).

DISCUSSION

This study traced the profile of the oncological male patients who sought a reproductive center to preserve fertility.

The high number of caucasians included in this study might be explained by the fact that 83.2% of Rio Grande do Sul population (Brazilian state where the study was conducted) belong to this group [6].

The data related to marital status and the presence of children might demonstrate the interest of childless young adults in maintaining their reproductive capacity. Also, education background seems to be correlated to fertility preservation demand; *id est*, the higher the education level, the greater the fertility preservation demand, which brings the reflection on cultural and financial barriers related to this field. According to Alvarenga et al., the socioeconomic status is directly connected to the difficulty of carrying out semen cryopreservation before the beginning of treatment [7].

Following the literature, testicular tumor and Hodgkin's/non-Hodgkin's lymphoma presented the most frequent tumor diagnosis. Although rare, testicular tumor in Brazil represents 5% of male tumors and occurs frequently in young people (20 to 40 years old), representing 60% of tumors in this age group [8].

Regarding the time between tumor diagnosis and cryopreservation, most patients took more than 30 days to do the first seminal collection. This fact might be explained by the state of disruption the patient experiences right after cancer diagnosis in which it is hard to think of fertility preservation and its importance [9].

The study also showed that some health professionals might be discussing with their patients on the risks of infertility after starting oncological treatment. The high percentage of patients performing seminal collection before starting therapy come as a suggestion to the aforementioned. A important mark which seems to have motivated oncologists to refer patients to fertility preservation was the published of The guidelines on clinical practices for fertility preservation in cancer patients, created by the American Society of Clinical Oncology in 2006 [10]. The guideline indicated the available fertility preservation options and the correct referral to specialized clinics [11]. However, according to our data, we cannot address any increase regarding the number of referred patients to fertility preservation, as during the four year of study, the number of cases were similar.

The most recent guideline of American Society of Clinical Oncology Clinical Practice also address

the importance of health professionals caring for adult and pediatric patients with cancer (including medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, pediatric oncologists, surgeons, and others) to discuss fertility preservation with all patients of reproductive age, if infertility is a potential risk of therapy, as early as possible before treatment starts [2].-

Finally, based on our results, and in order to motivate our health professionals to inform patients about the possibility of fertility preservation, we elaborate a simple algorithm based on the last American Society of Clinical Oncology Clinical guideline that is demonstrated in **Figure 4**.

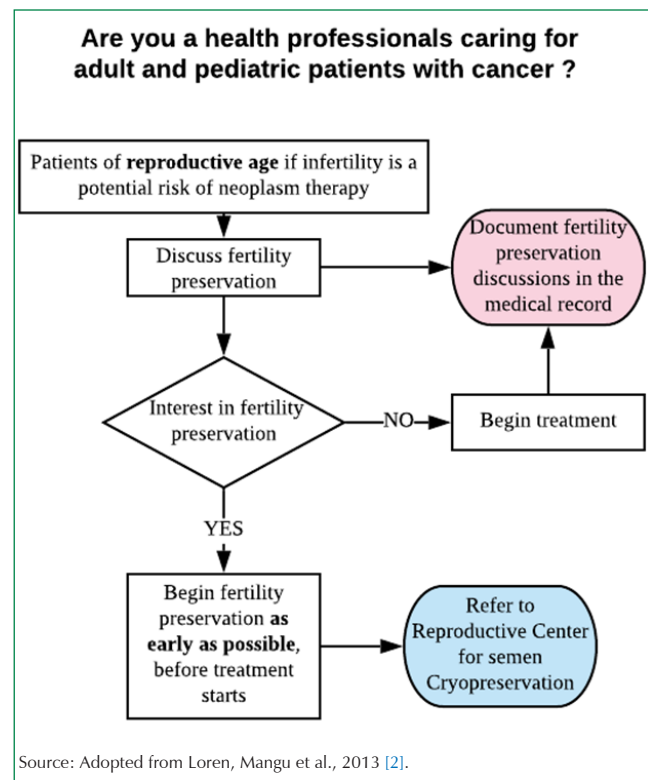


Figure 4. Fertility preservation assessment and discussion algorithm for patients with cancer.

CONCLUSION

It is important to highlight that the gametes cryopreservation is not performed by the Brazilian Unified Health System neither by private health insurances. Thus, men with a lower socioeconomic status might be in disadvantage in cases of family planning. However, it is known that new technologies

are coming and that in the future it is possible that a large part of the population could benefit from this type of treatment.

From now on, it is important to encourage health professionals to refer patients for gamete cryopreservation, prior to cancer treatment in order to contribute to reproductive health of patients.

NOTES

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Conflicts of interest disclosure

The authors declare no competing interests relevant to the content of this study.

Authors' contributions.

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve the version to be published.

Availability of data and responsibility for the results

All the authors declare to have had full access to the available data and they assume full responsibility for the integrity of these results.

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