Decision on fertility preservation in cancer patients: development of information materials for healthcare professionals

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<th>Journal:</th>
<th>Journal of Adolescent and Young Adult Oncology</th>
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<td>Manuscript ID:</td>
<td>JAYAO-2016-0064.R2</td>
</tr>
<tr>
<td>Manuscript Type:</td>
<td>Brief Report</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>n/a</td>
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</table>
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| Keyword:              | Chemotherapy, Fertility, Late Effects, Oncofertility, Supportive Care |
| Manuscript Keywords (Search Terms): | oncofertility, fertility preservation, information materials, decision support |
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Oncofertility: information for healthcare professionals

Keywords: fertility preservation, oncofertility, information materials, decision support
Abstract

Infertility is a potential side effect of cancer chemotherapy. As the number of AYA-aged survivors increases, future fertility becomes an important issue. However, many patients are not adequately informed and oncologists point the lack of information as a barrier to discussion. Our aim was to produce information materials, tailored to oncologists’ needs to promote and support discussion on infertility risk and fertility preservation with AYA-aged patients.

After literature review, information materials were successfully developed and are currently being distributed to healthcare professionals, in Portugal, with the collaboration of several national organizations. These information materials will contribute to shared, informed decisions regarding fertility preservation in AYA-aged patients.
Introduction

Infertility is a recognized potential adverse effect of several cancer treatments. In relation to chemotherapy, the degree of gonadal toxicity is influenced by several factors such as the nature of antineoplastic agents, total dose administered and patients' age. Additionally, the number of AYA-aged survivors is increasing, as a consequence of earlier diagnosis and significant progresses in cancer treatment. Besides the repercussions of the disease, these patients will have additional concerns related with the effects on their future fertility. Several studies document that future fertility is an important issue for cancer patients and survivors and, therefore, shared decision concerning fertility preservation (FP) must take place at the time of diagnosis. In this context, oncofertility, a term created in 2006 by Professor Teresa Woodruff, has emerged as a multidisciplinary field with the purpose to fulfil the needs of AYA-aged patients regarding their reproductive potential.

According to the recommendations of international organizations on cancer care, namely the European Society of Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO), healthcare providers should address infertility risks with all cancer patients treated during their reproductive years. Moreover, they must be prepared to discuss FP options or to refer potential patients to reproductive medicine specialists. Despite the above recommendations, several international studies indicate that professionals caring for cancer patients do not address these issues and a considerable proportion of AYA-aged patients is not informed on the possibilities regarding FP. The main reasons reported by health professionals were the lack of knowledge, access to reproduction specialists and information on FP options, especially
those remaining experimental. Patient-related factors such as bad prognosis, terminal
disease or the need to postpone treatments were also pointed to contribute.\textsuperscript{11}

In Portugal, the oncofertility area is taking its first steps. Nevertheless, a variety of
techniques for male and female FP are available at a few specialized institutions of the
National Healthcare System, including the \textit{Centro para a Preservação da Fertilidade}
(Centre for Fertility Preservation) of CHUC, EPE, in Coimbra.

Recently, the \textit{Sociedade Portuguesa de Medicina Reprodutiva} (Portuguese Society for
Reproductive Medicine) endorsed the organization of the 1\textsuperscript{st} and 2\textsuperscript{nd} Portuguese
Oncofertility Meetings, with the purpose of implementing an integrated national practice
concerning FP for cancer patients. In this process, the \textit{Centro para a Preservação da
Fertilidade} (Centre for Fertility Preservation) of CHUC, EPE, in Coimbra, has been at
the front line, actively promoting awareness of this new field and disseminating
information regarding infertility risks and FP options, both to AYA-aged patients and
healthcare professionals. One specific objective of this information program was the
production of information materials for Portuguese cancer care professionals, tailored to
the respective reported information needs, in order to promote and support discussion
with AYA-aged patients on the topics of infertility risks and FP.

\textbf{Methods}

\textbf{Assessment of information needs}

In order to identify worldwide reported information needs, a literature search was
conducted on Medline, through PubMed, combining the following MeSH terms:
\textit{Neoplasms}, \textit{Antineoplastic Agents/adverse effects}, \textit{Fertility/drug effects}, \textit{Fertility
For Peer Review Only/Not for Distribution

Preservation, Sperm banks, Health Knowledge, Practice and Attitude of Health Personnel. Quantitative studies reporting oncologists’ information needs concerning infertility risks and FP, or barriers to FP implementation were selected and critically evaluated.

Production of information

Information contents were selected to accomplish two main objectives: 1) to alert for the need to discuss infertility risks with patients and to help healthcare professionals estimating those risks; 2) to promote knowledge on the available male and female FP options. The latest published evidence on infertility risks associated with cancer treatments was identified through literature search, namely regarding mechanisms and adverse effects of cancer treatments on fertility, factors associated with infertility risk and tools available for risk calculation. Regarding FP techniques, current evidence-based information on clinical indications, time requisites, success rates, risks and advantages/disadvantages of each FP technique was gathered, also by literature search. Published clinical guidelines on FP in cancer patients were also identified.

A main booklet directed to clinicians working with cancer patients with comprehensive contents was prepared. This professional group presents the greatest information needs as they have the responsibility to initiate FP discussion with patients and referencing them to FP specialists. A booklet with summarized contents was also produced and intended to inform other healthcare professionals working in the cancer setting. This resumed booklet is also intended to primary care professionals, which many times make
the first contact with AYA cancer patients, so that they can promote awareness of the FP subject.

Results

Information needs

Twelve (12) published articles were selected and analyzed.\textsuperscript{13-24} Data on methods and relevant results (reported information needs, gaps in knowledge or barriers to FP discussion) was collected from each individual article (Table 1).

Information contents

All the identified information topics were included in the main booklet, named “Oncofertility. Fertility Preservation in Cancer Patients”. Information contents were organized in 4 main sections:

Section 1. Why the need for fertility preservation in cancer patients?

In this first section the relevance of oncofertility in the present context is discussed. Moreover, information on the topics of fertility outcomes of cancer survivors, evaluation of reproductive potential and (in)fertility markers, risk factors for infertility in cancer patients and infertility risks associated both with cancer and cancer treatments is also provided.

Section 2. How can cancer patients’ fertility be preserved?

This section includes the following sub-sections: Preserving fertility: which patients and when?; Male fertility preservation techniques; Female fertility preservation techniques
(organized according to their classification as established and experimental); Other FP procedures (ovarian transposition, GnRH agonists administration). For each FP technique information is provided regarding procedure, classification as established/experimental, indications (for whom and when), time requisites, success rates, risks for man/woman and offspring, ideal time for conception/pregnancy, using the cryopreserved cells/tissue and costs.

**Section 3. Questions & Answers**

For the most frequently reported topics, information was reinforced in a series of Questions & Answers (total of 15). Some examples are FP in estrogen-positive breast cancer (Which FP techniques are available for hormone-sensitive tumors?), FP in pre-pubertal patients (Which FP techniques are available for pre-pubertal patients?), time requisites for FP (Is there a need to postpone cancer treatments to allow for FP procedures in a cancer patient?), available guidelines (Are there national or international guidelines on FP in cancer patients?), patient referral (What is the procedure for referencing patients to a FP consultation?) or established versus experimental techniques (Which FP techniques are acknowledged as established medical practice?).

**Section 4. Information Tools**

A variety of practical tools were developed and included in this last section, including a compilation of electronic tools to estimate infertility risks, the infertility risk tables published by ASCO in 2013 (translated and adapted to Portuguese), a list of published international guidelines regarding FP in oncology and a comparative table of the female...
FP techniques. In addition, a list of recommended e-books and review articles was prepared.

The smaller booklet, called “Fertility Preservation in Cancer Patients” presents a similar general organization but summarized contents.

Information dissemination

The materials produced are being distributed with the collaboration of the Liga Portuguesa contra o Cancro (LPCC; Portuguese League Against Cancer), a nonprofit cancer patients organization, the Sociedade Portuguesa de Medicina Reprodutiva (SPMR; Portuguese Society of Reproductive Medicine), the Sociedade Portuguesa de Oncologia (SPO; Portuguese Society of Oncology) and the Ordem dos Farmacêuticos (OF; Portuguese Pharmaceutical Society). The LPCC published the summarized booklet and is disseminating both materials to primary care and cancer care health professionals, through its website and promotion campaigns. This smaller booklet is also being distributed to the Portuguese hospital and community pharmacists through the efforts of the OF. The comprehensive information booklet was printed with the support of the SPMR and is being distributed in cancer care institutions and to oncologists with the collaboration of the SPO. Moreover, all information contents of the produced materials are available through the website of the Centre for Fertility Preservation of CHUC, EPE (www.centropreservacaofertilidade.pt), in Portuguese.
Discussion

It is important to note that information materials directed to AYA-aged cancer patients were also developed in the context of this program, including decision aids to support the decision of preserving fertility (or not) and the choice of the FP technique (results to publish). Moreover, we would like to highlight the multidisciplinary context in which this project has been out, involving oncologists, reproductive medicine physicians, pharmacists, psychologists and the professional societies from the mentioned areas. This cooperation will certainly contribute to a wider dissemination of the developed information materials to the various intervenients in the process of cancer care and to a more effective clinical implementation.

Although the present information materials have been developed based on the internationally reported needs, the identified information topics are in accordance with the results from a locally applied questionnaire to a sample of 37 oncologists from two hospitals in the center region of Portugal (unpublished results). In this survey, topics regarding *types of cancer treatments associated to greater infertility risk, interference of FP techniques with cancer* and the *available FP techniques* were considered the most important information needs.

The developed information materials will support the role of cancer care professionals as patients' educators, increasing their participation in clinical decisions. Additionally, health professionals working in primary care settings can significantly raise awareness of this relevant subject, as they are in a privileged position to disseminate information to the general population.
The next step will be to disseminate these materials to other Portuguese language countries and the translation to English and French. Moreover, it is our intention to perform, in cooperation with the SPO, an evaluation study of cancer care clinicians’ perceptions on the relevance, reliability and completeness of contents and on the usefulness of this information for their clinical practice.

**Conclusions**

The opportune information of AYA-aged cancer patients on their risk of infertility and the possibilities concerning FP is recognized as a highly relevant issue, in the context of cancer survival quality of life. Our work confirms the significant information needs of oncologists on these subjects and, by fulfilling those needs, contributes to timely, shared and informed clinical decisions on FP.

**Acknowledgments**

This work was supported by a research grant from the *Liga Portuguesa contra o Cancro* (Grant LPCC/Celgene 2012).

**Author Disclosure Statement**

The authors state that there is no competing financial interest.
References


Table 1. Studies concerning information needs, gaps in knowledge and barriers to FP implementation used on the present work.

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Title</th>
<th>Methods (sample)</th>
<th>Information needs / gaps in knowledge / barriers to FP identified</th>
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<tbody>
<tr>
<td>13</td>
<td>Oncologists’ Attitudes and Practices Regarding Banking Sperm Before Cancer Treatment</td>
<td>A postal survey was sent to 718 oncology staff physicians and fellows (n=162).</td>
<td>FP options costs; FP facilities; risk of infertility in male versus female patients; treatment delay needed for FP</td>
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<tr>
<td>14</td>
<td>Fertility preservation in cancer survivors: a national survey of oncologists’ current knowledge, practice and attitudes</td>
<td>National online survey of oncologists (n=100).</td>
<td>FP options, specially testicular cryopreservation and ovarian cryopreservation; FP techniques success rates; FP in patients with hormonally sensitive malignancy</td>
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<td>15</td>
<td>Do doctors discuss fertility issues before they treat young patients with cancer?</td>
<td>Paediatric oncologists prospectively completed a data form for each new patient registered over a 12 month period (n=1030).</td>
<td>FP options in pre-pubertal patients; Experimental/established FP techniques; facilities available for FP</td>
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<tr>
<td>16</td>
<td>Strategies for Fertility Preservation after chemotherapy: Awareness among Irish cancer specialists</td>
<td>Online questionnaire to cancer specialists (n=50).</td>
<td>Success rates; low awareness of published guidelines; available facilities for FP; treatment delay needed for FP; FP in patients with estrogen receptor (ER) positive disease</td>
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<td>17</td>
<td>Oncologists’ confidence in knowledge of fertility issues for young women with cancer</td>
<td>National sample of medical oncologists, hematology/oncologists, radiation oncologists and gynecologic oncologists (n=344).</td>
<td>Infertility risk estimation; risks of pregnancy for the woman and the fetus; surgical techniques to protect the ovaries from radiation; new IVF stimulation protocols with less delay of cancer treatment or less estrogen exposure; cryopreservation of ovarian tissue and oocytes</td>
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<td>18</td>
<td>A nationwide survey of oncologists regarding treatment-related infertility and fertility preservation in female cancer patients</td>
<td>Email survey to a database of oncologists at the top 25 cancer hospitals as ranked by U.S. News &amp; World Report (n=249).</td>
<td>Risk of gonadotoxicity from specific regimens</td>
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<td>19</td>
<td>Who should be offered sperm banking for fertility preservation? A survey of UK oncologists and haematologists</td>
<td>Post questionnaire to all members of the Royal College of Radiotherapists’ Faculty of Oncology and the British Society for Haematology (n = 499).</td>
<td>Need to offer sperm banking to patients before they go through chemo- or radiotherapy; treatment delay needed for FP</td>
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<td>Study Title</td>
<td>Methodology</td>
<td>Key Findings</td>
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<td>20</td>
<td>Attitudes and Practices of Pediatric Oncology Providers Regarding Fertility Issues</td>
<td>Survey to healthcare providers in a pediatric hematology/oncology clinic (n=30).</td>
<td>Risks of infertility in boys versus girls; risks of ovarian failure in pre-pubertal versus post-pubertal girls; FP techniques in pre-pubertal girls; risk of cancer or birth defects in the offspring of cancer survivors</td>
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<tr>
<td>21</td>
<td>Fertility Preservation in Women Undergoing Treatment for Breast Cancer in the U.K.: A Questionnaire Study</td>
<td>Online questionnaire to surgeons, oncologists, and clinical nurse specialists who manage patients with breast cancer in the United Kingdom (n=306).</td>
<td>Treatment delay needed for FP; FP in patients with estrogen receptor (ER) positive disease; FP options available; interference of FP with the success of cancer treatment</td>
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<tr>
<td>22</td>
<td>Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancer</td>
<td>Survey by email to all members of a nationwide pediatric oncology subspecialty group (n=180).</td>
<td>FP in pre-pubertal patients; low awareness of published guidelines</td>
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<tr>
<td>23</td>
<td>Fertility preservation among patients with cancer: report of a French regional practical experience</td>
<td>Prospective survey amongst oncologists working in Provence Alpes Côte d'Azur region (n=225).</td>
<td>FP options available and indications</td>
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<td>24</td>
<td>Fertility Preservation Practices Among Ontario Oncologists</td>
<td>Questionnaire to Ontario physicians with specialties in medical oncology, radiation oncology, gynecologic oncology, and urology (n=152)</td>
<td>FP specialists for referral; FP costs</td>
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