Fertility in long-term cancer survivors

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The Assisted Reproductive Technologies (ART) Italian Register (est. 2005) has three major goals:

- The Register monitors and analyses all results and activities following ART-treatments in Italy.
- The Register collects suggestions and proposals from scientific societies and clinicians to optimize ART.
- The Register gives advice and information to all citizens in Italy.
- The Register is connected with the data collection system of European IVF Monitoring (EIM).

www.iss.it/rpma
An estimated 5 million babies have been born using ARTs since 1978.

On an average 27% of treatment cycles result in the birth of a baby (ESHRE, 2012)
In Italy, total and relative numbers of IVF babies born increased until 2011

<table>
<thead>
<tr>
<th>YEAR</th>
<th>BABIES BORN AFTER CONCEIVING NATURALLY*</th>
<th>BABIES BORN AFTER ART**</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>554.022</td>
<td>4.940</td>
<td>0,9</td>
</tr>
<tr>
<td>2006</td>
<td>560.010</td>
<td>7.507</td>
<td>1,3</td>
</tr>
<tr>
<td>2007</td>
<td>563.933</td>
<td>9.137</td>
<td>1,6</td>
</tr>
<tr>
<td>2008</td>
<td>576.659</td>
<td>10.212</td>
<td>1,8</td>
</tr>
<tr>
<td>2009</td>
<td>568.857</td>
<td>10.819</td>
<td>1,9</td>
</tr>
<tr>
<td>2010</td>
<td>561.944</td>
<td>12.506</td>
<td>2,2</td>
</tr>
<tr>
<td>2011</td>
<td>556.585</td>
<td>11.933</td>
<td>2,1</td>
</tr>
</tbody>
</table>

**Data may be underestimated due to losses to follow-up and cross borders reproductive care

*Source DemoISTAT
The developing ART technologies offer new perspectives to preserve Fertility in Cancer patients undergoing treatments

Cancer patients survive at increasing rates, but cancer treatment often leads to reduced fertility, sexual dysfunctions and endocrinology complications.
Cancer patients are not sufficiently informed about fertility preservation.

**FIGURE 1**

How often do you refer patients to a reproductive endocrinologist or obstetrician/gynecologist who specializes in fertility?

- **Never**: 17.8%
- **Rarely**: 43.3%
- **Usually**: 33.2%
- **Always**: 5.8%

Why oncologists do not discuss infertility:

- Insufficient time to counsel in life threatening situation
- Data regarding the risks of infertility are not known
- The importance of fertility is not an important priority to the physician
- Belief that the cost of fertility preservation is high.
- Patient’s cancer prognosis is poor.
- Belief that patients are not interested for other reasons.
- Emotional discomfort with discussing fertility issues.
In USA guidelines to preserve fertility exist from 2006, in Italy since 2013.

Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine
American Society for Reproductive Medicine, Birmingham, Alabama

Patients preparing to undergo gonadotoxic medical therapy or radiation therapy or gonadectomy should be provided with prompt counseling regarding available options for fertility preservation. Fertility preservation can best be provided by comprehensive programs designed and equipped to confront the unique challenges facing these patients. (Fertil Steril 2013;100:1214-23. ©2013 by American Society for Reproductive Medicine)

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertsterfforum.com/asrmpraccom-fertility-preservation-chemotherapy-cancer/
Increased survival of breast cancer patients between 20 to 44 years of age (data from ARTIUM)

- Breast cancer patients 2000-2004: 84.3%
- Breast cancer patients 2005-2009: 86.5%
Established techniques to preserve fertility are:

Sperm banking is of key importance

Random-start controlled ovarian hyperstimulation for emergency fertility preservation in letrozole cycles

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Conclusions: One out of five PCA patients would bank sperm before RP. Most patients considered it necessary to establish a dedicated service for preoperative sperm cryopreservation, regardless of their own motivation to bank sperm. (Fertil Steril 2013;100:367–72. ©2013 by American Society for Reproductive Medicine.)

Key Words: Fertility, infertility, prostate cancer, radical prostatectomy, sperm banking

Discuss: You can discuss this article with its authors and with other ASRM members at http://
Experimental techniques to preserve fertility are:

- Cryopreservation of testicular tissue
- Cryopreservation of ovarian tissue
From 2005 to 2011

- 20,016 cycles with cryopreserved oocytes have been performed
- This number represents 5.8% of all IVF-cycles performed in the same period

The cycles with cryopreserved oocytes resulted in 2,405 pregnancies and 1,674 babies born

- 2.7% of babies from ART were born thanks to cryopreserved oocytes
Other ways to preserve fertility aside from those offer by ART:

- Pelvic shielding during radiation therapy
- Ovarian transposition
- Ovarian-sparing (conservative) surgery
- Removal of the cervix but not the uterus
- Medical treatment of endometrial cancer
- Treatment with gonadotropin-releasing hormone (GnRH) agonists
Pregnancy after breast cancer treatment has a positive effect on the overall outcome

- breast cancer survival is not negatively affected by pregnancy
- There may be a slight protective effect
Pregnant patients were at less risk of recurrence and more mortality free.
Our first multicentric project was conducted with many different ART center in Italy

“Fertility preservation in cancer patients or in patients at risk of iatrogen infertility” 2009-2010

A collaboration between

Registro Nazionale della PMA Istituto Superiore di Sanità - Roma

Azienda Ospedaliera San Giuseppe Moscati di Avellino – Unità di Fisiopatologia della Riproduzione

E.O. Ospedali «Galliera» di Genova Struttura Semplice di Fisiopatologia Preconcezionale e Prenatale

Dipartimento di Discipline Ginecologiche ed Ostetriche Università di Torino, Ospedale Sant’Anna

Azienda Ospedaliera San Martino e Cliniche Universitarie convenzionate Clinica Ostetrica e Ginecologica, Università di Genova

Ospedale Santa Maria Nuova di Reggio Emilia Unità Operativa di Ginecologia ed Ostetricia

Centro di Biologia della Riproduzione - Palermo

Istituto Europeo di Oncologia - Milano Unità di Fertilità e procreazione in Oncologia
595 samples were cryopreserved (2009-2010)

- 345 patients cryopreserved sperm
  235 patients cryopreserved oocytes
  15 patients cryopreserved ovarian tissue

- Studies to determine the best cryopreservation protocol for ovarian tissues

- Studies on the damage caused by oocyte cryopreservation induced by slow freezing
A brochure to inform patients was edited

Having children after cancer is possible, just arrange it on time
The second multicentric project was between Institutions and Medicine Structure

Strategies for spreading the awareness of fertility preservation in cancer patients: an integrated approach between reproductive medicine and institutions 2010-2012

ISS Registro Nazionale della PMA

Ospedale San Raffaele di Milano

AIMaC Associazione Italiana Malati di Cancro
Goals and tools of the multicentric study

- Identifying patients in need of fertility preservation
- Assessment of the information quality provided to patients

Gynecologic, Oncologist, Psychologist Education

Information, Dissemination

Training courses at Istituto Superiore di Sanità
3th October 2011
21st March 2012

Pamphlets / brochures posters / flyers
Eligible patients of survey: 157

Of all cancer patients 56.7% expressed the desire to have children.
Information received from patients:

- Potential risks of infertility after cancer treatments: 77.6%
- Potential strategies for preserving fertility: 57.8%
- Chance of becoming pregnant after cancer treatments: 60.1%
- Risks of cancer recurrence after pregnancy: 56.3%
- Potential harmful effects in the fetus after cancer treatments: 56.3%

Only half of the study population (57.8% of 157) were informed on fertility preservation strategies.
Of all cancer patients 46.6% were satisfied with the information received.

Satisfaction with the information provided on fertility preservation by type of cancer

- All patients: 46.6% satisfied, 10.2% neutral, 43.2% dissatisfied
- Breast: 49.2% satisfied, 11.5% neutral, 39.3% dissatisfied
- Lymphoma/Leukemia: 25.0% satisfied, 75.0% dissatisfied
- Ovarian: 80.0% satisfied
- Melanoma: 100.0% satisfied
- Cervical: 100.0% satisfied
- Others: 46.2% satisfied, 15.4% neutral, 38.5% dissatisfied
Infertility, endocrine metabolic complications and sexual dysfunction in men and women suffering from cancer and hematological diseases: monitoring and treatment in the short and long term 2012-2014

Collaboration with:

ISS Registro Nazionale della PMA

IRCCS Istituto Clinico Humanitas, Rozzano Milano

RAO Ospedale Umberto I Siracusa
The project is dedicated to the care of cancer patients

- provide counseling for sexual problems
- provide help for patients at risk for iatrogenic infertility
- 27 patients were enrolled (21 females and 6 males). Of those 11 patients chose to preserve their fertility
In 2013/14 all Italian ART centers were contacted to report on their activity with cancer patients

Survey carried out in 2013/2014 by the ART Register
Survey started in November 2013

201 ART centers were contacted

65 ART centers (32.3%) participated

4 do not offer services for cancer patients

61 offer ART treatments for cancer patients
61 ART centers perform fertility preservation treatments

- 56 ART centers (91,0%) offer **oocytes** cryopreservation
- 24 ART centers (39.3%) offer **ovarian tissue** cryopreservation
- 58 ART centers (95,0%) offer **sperm** cryopreservation

61 ART centers collected samples
Map of 61 ART centers that collected samples from cancer patients by type of service

Public Centers (NHS) 28

Private Centers 33
SUMMARY

• In summary cancer patients in Italy are still not sufficiently informed about the possibilities of fertility preservation and

• the services of ART are not offered in all regions of Italy, therefore the cooperation between our centers have to be improved considerably and the region should invest more effort to provide this important service to patients.
Thank you for your attention

For further information visit:

www.iss.it/rpma
Survivorship: Sexual Dysfunction (Male), Version 1.2013

Crystal S. Denlinger, MD, Robert W. Carlson, MD, Madhuri Are, MD, K. Scott Baker, MD, MS, Elizabeth Davis, MD, Stephen B. Edge, MD, Debra L. Friedman, MD, MS, Mindy Goldman, MD, Lee Jones, PhD, Allison King, MD, Elizabeth Kvale, MD, Terry S. Langbaum, MAS, Jennifer A. Ligibel, MD, Mary S. McCabe, RN, BS, MS, Kevin T. McVary, MD, Michelle Melisko, MD, Jose G. Montoya, MD, Kathi Mooney, RN, PhD, Mary Ann Morgan, PhD, FNP–BC, Tracey O’Connor, MD, Electra D. Paskett, PhD, Muhammad Raza, MD, Karen L. Syrjala, PhD, Susan G. Urba, MD, Mark T. Wakabayashi, MD, MPH, Phyllis Zee, MD, Nicole McMillian, MS and Deborah Freedman–Cass, PhD

Abstract

Various anticancer treatments, especially those directed toward the pelvis, can damage blood vessels and reduce circulation of blood to the penis and/or damage the autonomic nervous system, resulting in higher rates of erectile dysfunction in survivors than in the general population. In addition, hormonal therapy can contribute to sexual problems, as can depression and anxiety, which are common in cancer survivors. This section of the NCCN Guidelines for Survivorship provides screening, evaluation, and treatment recommendations for male sexual problems, namely erectile dysfunction.

Survivorship: Sexual Dysfunction (Female), Version 1.2013

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Abstract

Cancer treatment, especially hormonal therapy and therapy directed toward the pelvis, can contribute to sexual problems, as can depression and anxiety, which are common in cancer survivors. Thus, sexual dysfunction is common in survivors and can cause increased distress and have a significant negative impact on quality of life. This section of the NCCN Guidelines for Survivorship provides screening, evaluation, and treatment recommendations for female sexual problems, including those related to sexual desire, arousal, orgasm, and pain.
Random-start controlled ovarian hyperstimulation for emergency fertility preservation in letrozole cycles

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