International Federation of Fertility Societies

Global Standards of Infertility Care

Standard 11

Fertility Preservation

Name	Fertility preservation
Version number	11.0/IFFS/Standards
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Date of first release	June2012
Date approved by IFFS	October 2012
Date of review	October 2015

Introduction

The goal of IFFS Practice Standards is to provide policy and decision-makers and the clinical and scientific community with a set of recommendations that can be used as a basis for developing or revising institutional or national guidelines on selected practice recommendations for infertility practice.

The document addresses minimal standards of practice but does not provide rigid guidelines but rather gives recommendations that provide the basis for rationalizing the provision of infertility services in view of the most up-to-date information available.

Because country situations and programme environments vary so greatly, it is inappropriate to set firm international guidelines on infertility practice. However, it is expected that institutional and national programmes will use these guidance documents for updating or developing their own infertility guidelines in the light of their national health policies, needs, priorities and resources. The intent is to help improve access to, quality of, and safety of infertility and assisted conception services. These improvements must be made within the context of users' informed choice and medical safety. Adaptation is not always an easy task and is best done by those well-acquainted with prevailing health conditions, behaviours, and cultures.

Rationale

There are an extensive number of scientific publications about the benefits of preserving fertility in cancer patients; either in women, men, children or adolescents, regardless of the chosen procedure. Different techniques and research lines raise questions about their effectiveness and safety. It is clear that, from this point of view, fertility preservation is generally accepted.

Due to the advances of modern medicine, the population of young people who are cancer survivors is growing. It is widely considered to be good medical practice to talk about fertility preservation techniques before the patient undergoes cancer treatment. In benign situations, in which the patient will undergo chemotherapy or radiotherapy treatments, fertility preservation methods should also be offered. Chemotherapy agents diminish gonadal reserve: in women this produces follicular apoptosis and cortical fibrosis; in men this produces apoptosis and fibrosis. Healthy women who choose to postpone their fertility due to other reasons can also take advantage of these techniques [1-11]

Scope of this guidance

This guidance covers several assisted reproductive technologies with the aim of preserving fertility. The techniques included in this guidance are:

- Ejaculated Sperm cryopreservation
- Testicular tissue cryopreservation
- Embryo and Oocyte cryopreservation
- Solid ovarian tissue cryopreservation

The scope of this guidance does not include a review of the possible effects on ovarian function of oncology treatment, laboratory techniques involved in gamete cryopreservation or the legal and ethical considerations of gamete storage.

The conditions for which these techniques may be considered include:

1. Men and women with cancer

2. Women at risk of premature ovarian insufficiency (POI) due to:
    a. Radiotherapy and chemotherapy in non-malignancies e.g. rheumatoid arthritis and auto-immune renal disease
    b. Genetic aberrations e.g. Turner's syndrome, genetic mutations, Kallman's syndrome (ZFX, FRAXA)
    c. Auto-immune ovarian damage
    d. Iatrogenic complications after ovarian surgery – how to you preserve fertility in this case – is the damage already done
    e. Those at risk due to environmental factors[12]
3. Men at risk of fertility loss due to
    a. occupational hazards[13]
    b. Non cancer medical conditions e.g. auto-immune diseases that require gonadotoxic therapy
4. Men who are considering permanent contraception by vasectomy

Assessment

1. The impact of the oncological treatment depends on the previous ovarian reserve, age of patient, chemotherapy agent and dosage schedule.

2. The evaluation of ovarian reserve prior to oncological treatment should include as a minimum FSH and Oestradiol. Other tests such as ultrasound assessment of antral follicle count and AMH are helpful if resources permit.

3. A semen analysis should be undertaken prior to men undergoing gonadotoxic therapy.

Effectiveness and Safety

1. In the last three years, several publications on **oocyte cryopreservation** have shown oocyte **survival rates** exceeding 90% regardless of the cryopreservation method used[21.] Pregnancy and **live birth rates** exceeding 50% have been reported in women who preserve their oocytes under 30.

2. Current evidence to date on the incidence of congenital anomalies arising in children from the use of cryopreserved embryos and gametes is reassuring. Further data collection is necessary to confirm this. [22-25]

3. Ovarian tissue cryopreservation has produced too few pregnancies at the time of writing to make recommendations for the effectiveness or safety of this procedure.[11, 26]

4. The success reported in recent years should stimulate a **new debate** on the subject as the suggestions, guidelines, and recommendations are behind the times and outdated. It is time to **revisit this subject** and ask the committees for a new evaluation and a general discussion with support from the international community.

Recommendations for Practice

Fertility Preservation Procedures for Men

1. Men who are advised to have chemotherapy treatment for cancer should routinely be offered sperm cryopreservation and storage as this process is well established and offers an excellent chance of preserving fertility. [15]

2. Men who are considering vasectomy may also wish to consider fertility preservation. In these cases if resources permit should be advised about the potential for semen cryopreservation and storage.

3. The techniques include sperm cryopreservation, testicular sperm extraction and testicular tissue freezing [14] Sperm cryopreservation is the most widely used and it is offered in many fertility clinics as a standard procedure. It is the most accepted technique for post-pubertal boys.

4. In prepuberal boys, sperm tissue extraction and testicular tissue cryopreservation are advised as in these cases mature sperm cannot be found in their ejaculate. In this client group specialist counselling and support is recommended.

5. Specific processes should be in place for detailed counselling, obtaining of consent and future contact tracing because of the likelihood of long term storage of material and the life limiting nature of the condition underlying the need for fertility preservation.

Current research includes attempts to obtain spermatogonial stem cells from embryonic stem cells to germ cells and work to create embryonic stem cells from spermatogonial adult male testicular tissue.[14] Other new and promising techniques to restore male fertility exist such as stem cells to germ cell maturation, germ cell transplantation, and germ cell maturation but these are experimental and as yet ***there is insufficient evidence to recommend these techniques***.

Fertility Preservation Procedures for Women

1. Women in the reproductive age group who are to undergo treatment known to damage ovarian function should be offered discussion about fertility preservation.

2. When the underlying condition is cancer the window of opportunity for fertility preservation is short and access to the reproductive medicine team should take account of this.

3. Management should involve multidisciplinary discussions between the Reproductive Medicine specialists and physicians / oncologists involved in the (potentially) fertility compromising treatment to insure a clear understanding of the likely impact on ovarian function of the treatment proposed.

4. Specific processes should be in place for detailed counselling, obtaining of consent and future contact tracing because of the likelihood of long term storage of material and the life limiting nature of the condition underlying the need for fertility preservation.

5. The two most common techniques for fertility preservation are:

    a. **Embryo cryopreservation**
    This is the most commonly applied procedure for preserving fertility in women who are in an established relationship or chose to use donor sperm and who have sufficient ovarian reserve. Its effectiveness is established and is related to the women's age.

    b. **Oocyte Cryopreservation**
    Oocyte cryopreservation has now become an established technique with defined methodology. There is an acceptable success rate particularly in younger women. Vitrification is becoming increasingly common for oocyte cryopreservation and may account for the improved outcomes following the use of thawed oocytes. However, at the time of writing there is insufficient evidence to make recommendations about the freezing methodology. [18]

O**varian tissue cryopreservation**

In women faced with pelvic surgery for certain benign gynaecological conditions and some cancer treatments this option may be considered. Details of the different techniques available for solid ovarian tissue cryopreservation is beyond the scope of this guidance and include segmental tissue and whole ovary cryopreservation with subsequent autologous transplantation. ***Presently, there are too few published births using these techniques to recommend practice in this area.*** [16,17] This is the only procedure capable of preserving fertility in pre-puberal girls, although this procedure is experimental.

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