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Fertility preservation in cancer patients: The global framework

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ABSTRACT

Cancer treatment is the most frequent cause of reduced fertility in cancer patients, with up to 80% of survivors affected. None of the established or experimental fertility preservation methods can assure parenthood, rather they may provide a future opportunity to overcome treatment induced sterility. Around 70–75% of young cancer survivors are interested in parenthood but the numbers of patients who access fertility preservation techniques prior treatment are significantly lower. Moreover, despite existing guidelines, healthcare professionals do not address fertility preservation issues adequately. Lack of time and knowledge about existing options, delay in potentially useful treatment, patient's age, partnership status, existing children, sexual orientation and socioeconomic situation are the main barriers to effective fertility preservation. Patient's fears, expectations and priorities shaped by personal values have to be addressed in the framework of medical necessities, realistic survival probabilities, socio-cultural environment and resources availability. We call for a need of patient centred fertility counselling within a framework that should include patients understanding of medical aspects of their cancer, realistic fertility preservation options, preferences based on personal values and goals. Optional support services could also include legal guidance, psychological and spiritual support and financial counselling.

Introduction

Cancer is predominantly associated with older age, but it also affects children, adolescents and young adults. Survival rates are known to be the highest for patients aged between 15 and 44 [1], with 5-years survival ranging from 60 to 82% according to age, tumour site and country of treatment [1–6]. Cancer therapies, nevertheless effective, often come with undesirable side effects, some of which are for a lifetime. Among these, infertility may affect up to 80% of cancer survivors as a result of treatments [7].

Cancer itself is rarely a direct cause of infertility [8,9]. Chemotherapy, radiotherapy or surgical removal of reproductive organs are the most frequent determinants of infertility in cancer survivors [10].

Cancer treatment effects on fertility

Male germ cells are sensitive to injury caused by cytotoxic drugs [11]. Leydig cells are resistant to chemotherapy [8], thus infertility rather than impaired sexual function is more frequently reported after oncological treatments. In females, ability to conceive can be affected by previous exposure to chemotherapy, radiotherapy or surgery. Adequate follicular reserve, a functioning hypothalamic-pituitary-ovarian axis and a normal uterus are all necessary for a normal pregnancy [8]. Many chemotherapeutic agents are gonadotoxic, but alkylating agents pose the highest risk of permanent infertility [12]. Moreover, oocytes are extremely sensitive to ionizing radiation, with direct correlation with dose and increasing patient's age [12]. Cranial radiation, affecting the hypothalamic-pituitary axis, may also impair fertility [12,13].

Established and experimental methods can be used to preserve fertility. None of them assure parenthood after cancer, thus unrealistic expectations or false hopes should not be given to the patients [14]. The most established and clinically approved methods for fertility preservation are sperm cryopreservation for men; embryo and oocytes cryopreservation and ovarian transposition for women [15].

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Fertility preservation options for male patients

Sperm cryopreservation is the only established method for male fertility preservation [15]. Usually 3 semen samples are frozen, with at least 48-h abstinence periods between each collection. However, if there is an urgent need to start cancer therapy, fewer samples can be cryopreserved [16]. Single intracytoplasmic sperm injection (ICSI) is now commonly used in assisted reproduction, thus allowing the successful use of samples with few spermatozoa [16,17]. It has been reported that 21% of Hodgkin lymphoma survivors who cryopreserved sperm prior their treatment used it [18] and a live birth using sperm frozen 21 years before has been described [19]. In prepubertal boys, testicular tissue cryopreservation is the only possibility for fertility preservation. Spermatogonial diploid stem cells could possibly develop into mature cells after transplantation [16], but this method still remains experimental at the present time [20]. There is also a concern that with testicular tissue auto-transplant the malignancy can be reseeded [21].

Fertility preservation options for female patients

Embryos cryopreservation is the most established and successful method for female fertility preservation. It requires delaying cancer treatment by 2–3 weeks and the availability of a partner. If a partner is not available or embryo cryopreservation is not permitted by law, oocytes cryopreservation is a valid alternative [16]. Oocyte cryopreservation is not considered experimental since 2013, when the American Society of Clinical Oncology (ASCO) and the European Society of Medical Oncology (ESMO) [22,23] endorsed this procedure. More than 1000 births have been reported worldwide from cryopreserved oocytes [22,24]. Summary of different guidelines and their implications on fertility preservation practices are given in Table 1.

Both embryo and oocyte cryopreservation need an ovarian stimulation with gonadotropins and oocyte harvesting. In oestrogen dependent tumours, there is concern that ovarian stimulation may increase disease recurrence [16]. The concomitant administration of Letrozole reduces oestrogen peak and data, albeit based on few trials with short follow up, demonstrate that disease free survival was similar in women who had ovarian stimulation, compared with women who did not have it [25]. Ovarian transposition (also called oophoropexy or ovarian suspension) is the surgical translocation of ovaries from the irradiation field in pelvic area. This method does not protect against chemotherapy or whole-body irradiation [16].

Ovarian suppression using gonadotropin-releasing hormone agonists for fertility preservation remains controversial. There is no sufficient evidence that it protects gonadal function from gonadotoxic agents [22].

Ovarian tissue cryopreservation follows laparoscopic removal of ovarian cortical tissue which is then cryopreserved and transplanted back when conception is desired [16]. Ovarian grafts can be transplanted into the pelvis or subcutaneously, where oocytes might be picked up after maturation [26]. There has not been pregnancies achieved using frozen-thawed ovarian tissue taken from prepubertal girls [27], possibly for the high numbers of abnormal non-growing oocytes [28]. As for testicular tissue auto-transplantation, ovarian tissue auto-transplantation may cause tumour reseeding if the graft is contaminated by malignant cells.

Twenty-eight live pregnancies have been achieved with orthotopic ovarian tissue transplant from patients with haematological malignancies and breast cancer [29]. Currently about 100 centres worldwide perform ovarian tissue cryopreservation [13]. Whole ovary cryopreservation remains experimental, and no live births have been achieved using this technique. It has been reported that 2 babies were born from whole ovary transplantation in monozygotic twin donor [30]. Therefore, some authors suggest that cryopreservation and retransplantation of whole ovary is promising and further research should be encouraged [31].

Moreover, there is a group of oncology patients known as 'previvors' and they deserve a special attention in cancer treatment and fertility preservation debate. These patients have cancer history running in their families and are at increased risk to develop cancer early in their lives. They have to think about prophylactic therapies even before being diagnosed with cancer. Such prevention strategies are suggested for women who are BRCA1 and BRCA2 mutation carriers and have high risk of developing breast or ovarian cancer [32]. Women of African ancestry under age of 45 have an elevated risk of breast cancer at young age compared to Caucasian women and their cancers are more aggressive that present as oestrogen receptor negative tumours [33]. It is suggested that these different groups of patients might have special needs that are unmet during fertility preservation counselling [34].

What do patients think about fertility preservation and what happens in the real world?

Retrospective surveys of cancer patients' views suggest that the majority have a strong desire to be informed about fertility preservation and available options [31,38–40]. Moreover, concerns about infertility are not limited to patients who are young and childless or/and have a partner [41]. It has been reported that up to 70–75% of young cancer survivors would like to have a child [39,42] with up to 29% of women refusing life saving treatment because of fear to become infertile [42], including a case reports where refused therapy lead to foetal and maternal death [43]. However, significantly fewer patients actually proceed with fertility preservation procedures. Despite proven clinical and psychological benefit [41,44] and recommendations that cancer patients should be routinely asked about their interest to preserve fertility before starting cancer treatment (Table 1), nearly half of patients are not given information about the impact of cancer treatment on their future fertility.

Studies on patients' attitudes and fertility preservation choices are being conducted worldwide. In Table 2 we summarized studies from USA, Canada, Sweden and Germany which report patient attitudes and the choices they subsequently made in order to preserve fertility. It is important to note that these reports vary in sample size and methodology. Response rate is often less than half of eligible participants which could mean that only patients who were concerned about fertility chose to answer the questions. Moreover, sample sizes are often too small to make valid generalizations for all cancer patients. Nonetheless, these studies revealed some important aspects in fertility preservation practices. First, majority of cancer patients regardless of final decision find fertility consultations an important part of their treatment planning. Second, there are still high numbers of patients who have not received any kind of fertility preservation consultation. This tendency seems to be apparent among female patients [39,45] and especially among racial minorities in the USA [34]. UK study of women with breast cancer who were childless concluded that although guidelines are available, many women were not given adequate information or offered treatments or interventions to preserve fertility [38]. This leads to the third point that women preserve fertility less often than men.

For instance, the study from Germany reports that only 40% of cancer patients who wanted children in the future underwent fertility preservation [39]. Results from Swedish cancer survivors' survey reveal large gender disparities in received information about treatment impact on fertility, with 80% of male and 48% of

Table 1
Guidelines for fertility preservation in cancer patients.

Releasing body; year	Scope	Main statements regarding toxicity of cancer therapy, fertility preservation (FP) and future procreation	References
American Society for Reproductive Medicine – ASRM; 2013	All cancer patients	Clinicians should inform patients about FP options and future reproduction before gonadotoxic treatment begins Concerns about welfare of resulting offspring are not sufficient reasons to deny assistance in reproduction Parents may act to preserve fertility for minors (assent and likeliness to provide future benefit) Preimplantation genetic diagnosis (PGD) to avoid offspring inheriting high risk of cancer is acceptable Patients should have access to mental health, genetic and financial counsellors	[35]
American Society of Clinical Oncology – ASCO; 2013	All cancer patients	Discuss FP with all patients of reproductive age (with parents or guardians of children and adolescents) Refer interested (and ambivalent) patients to fertility specialist Address FP before treatment starts Document FP discussion in medical records Answer basic questions about FP and its impact on cancer treatment Refer patients to psychosocial providers if patients experience distress Encourage patients to participate in registries and clinical studies	[22]
National Comprehensive Cancer Network – NCCN, USA; 2014	Adolescents and young adult (15–39)	Fertility preservation should be an integral part of cancer management The use of contraception should be discussed with all women before initiation of treatment Women diagnosed with cancer during pregnancy require individualised treatment by multidisciplinary team All patients should have access to age-appropriate supportive care and medical subspecialty services	[36]
European Society of Medical Oncology – ESMO (endorsed by Japanese Society of Medical Oncology – JSMO); 2013	Cancer patients in reproductive age	Male: Sperm banking should be planned before treatment initiation Female: Young women desiring future fertility should be counselled on available fertility preservation options before starting anti-cancer treatment	[23]
European Society of Breast Cancer Specialists – EUSOMA; 2014	Young women (under 40)	Fertility issues should always be discussed before the start of any breast cancer therapy Discussion should allow time for reflection and involve partner, if present Early referral to reproductive endocrinologist is warranted	[37]
European Society of Human Reproduction and Embryology – ESHRE; publishes ethical considerations from 2001	Does not have a guideline specifically for oncology patients	Provides guidelines relevant to fertility preservation in oncology: cryopreservation, PGD, posthumous reproduction, infertility treatment, wellbeing of ART children, distinction between established and experimental treatment (concerning oocyte cryopreservation) at http://www.eshre.eu	

women informed. While 54% of male patients banked frozen sperm, only 2% of women underwent fertility preservation [45]. There are only scarce data available from countries other than those in North America and Europe, but it is likely that fertility preservation issues might share a lot of similarities worldwide. For instance, in Saudi Arabia less than 20% male patients are referred to fertility specialist [46], which suggests that even male patients do not always take the full advantage of fertility preservation options.

Another study has been published recently comparing attitudes towards fertility loss among young breast cancer patients. This study collected data from Western and Eastern Europe, South Africa, Middle East and South America concluding that 59% of patients wanted to have children in the future but cure was the first priority and only less than 10% would accept lower chances of survival to preserve fertility [47]. These numbers suggest that the importance of fertility could have been overestimated but some other studies show that having a child could have a positive effect on cancer survivors helping them to stay well, feel complete and look forward to the future [47]. However, even women with positive attitudes about having children after cancer have fears that possible pregnancy would increase chances for cancer recurrence or transmitting the cancer risk to the future child [47,48]. On the other hand patients who already have children might focus more on survival than fertility preservation [40,42] and as a result might be less likely to be offered fertility preservation consultation [46,49]. Therefore, discussing cancer treatment implications on fertility and possible fertility preservation options as well as providing patients with decisional support would significantly help to improve cancer care and benefit the patients in any country.

Healthcare professionals' attitudes towards fertility consultation in oncology patients

It is suggested that individual plans for fertility preservation must take into account both patient's priorities and medical necessities [15], especially when healthcare systems are run on limited resources. There is also a need to create a functional infrastructure for oncofertility services. However, even countries with established services for patients face problems. For instance, in the United States fertility preservation services are currently available to most patients who are under the age of 45 [32] but some still have restricted access to care due to their socioeconomic situation, insurance plan or geographical location [33]. Fertility centres in Canada are keen about working together with other healthcare providers to offer fertility preservation services for cancer patients [48]. However, despite all required components are present in the Canadian system, their coordinated functioning remains challenging [52].

Despite existing fertility preservation methods for both men and women, patient wishes to be informed about fertility preservation options and a number of guidelines how fertility consultations should be addressed, physicians are still misled by their personal biases when it comes to discussing fertility preservation during consultations. We identified studies from UK, Japan, Saudi Arabia, Turkey, Iran and the USA reporting fertility preservation practices

Table 2
Cancer patients' attitudes towards fertility preservation (FP).

Country; publication year	Participants; type of study	Attitudes, expectations, experiences regarding FP (%)	Number of patients who used FP and methods (%)	References
Texas, USA; 2012	33 African American breast cancer survivors under age of 45; semi-structured phone interviews	45% reported retrospectively that they had wanted a child at the time of diagnosis 48% did not remember having discussed FP with a doctor 14% of those who had chemotherapy have been offered FP	1 patient froze embryos and oocytes 1 patient froze oocytes 4 patients became pregnant after cancer treatment 1 sought IVF treatment 2 adopted children after their cancer	[34]
USA; 2014	620 women aged 17–40 newly diagnosed with early breast cancer; multicenter cohort study, survey by mail	68% discussed fertility issues before starting the therapy 51% were concerned about becoming infertile 26% concerns about fertility affected their treatment decisions	10% pursued FP 7% embryo cryopreservation 1% oocyte cryopreservation 3% received gonadotropin-releasing hormone agonist (GnRH-a)	[50]
Canada; 2012	27 breast cancer patients aged 24–41; anonymous mail questionnaire	56% of FP consultations were made after surgery before chemotherapy 33% of FP consultations were made before surgery 85% consultations were made within a week of referral	56% (15 patients) underwent FP 9 patients froze embryos 6 froze eggs alone 2 ovarian suppression	[51]
Canada; 2012	41 female cancer patients aged 24–42, majority breast cancer, others ovarian cancer, lymphoma, brain cancer, Hodgkin's, carcinoma, leukaemia; mail questionnaire	97.6% regardless of final decision said that it was important to be seen by reproductive specialist	31.7% proceeded with IVF for cryopreservation (13 patients) 6 were planning to initiate pregnancy soon	[41]
Sweden; 2012	484 survivors aged 18–45 at diagnosis who had lymphoma, acute leukaemia, testicular cancer, ovarian cancer or female breast cancer treated with chemotherapy; postal questionnaire	80% male patients received information about treatment impact on fertility 68% male patients received information about FP 48% female patients received information about treatment impact on fertility 14% female patients received information on FP	54% male patients banked sperm 2% female patients underwent FP including embryo and oocyte cryopreservation, ovarian suppression, radiation shielding of gonads	[45]
Germany; 2014	149 cancer patients aged 18–45; questionnaire	74% had a desire to have children at the time of diagnosis 60% discussed fertility with oncologists 20% discussed fertility with specialist	56% male undergone sperm cryopreservation 31% female preserved fertility: 4 oocyte cryopreservation 5 ovarian tissue cryopreservation 13 took medication	[39]

and factors influencing physician's decision to discuss fertility preservation with their patients (Table 3).

Only British and American physicians are reported to discuss fertility issues with their patients on most occasions [53,54]. However, American physicians tend to have more biases based on social issues, gender and racial factors and medical prognosis compared to the UK physicians [53]. In other countries fertility preservation consultations do not occur on regular basis and referrals to fertility specialists are even lower [46,55,56]. General tendency reported in most studies is that physicians are concerned with patient's prognosis [49,53], type of cancer [46,53] and reluctance to delay the start of treatment [49,57]. Lack of knowledge about fertility preservation and time constraints were also among the reasons why fertility preservation was not addressed by British, Japanese, Turkish and Iranian physicians (Table 3).

As for patient surveys, also physicians' surveys vary in sample sizes and response rates. However, the methodology is more coherent and studies could be legitimately compared: postal or online questionnaires are used, attitudes, consultation and further referral practices are studied, reasons why fertility preservation issues are not discussed are addressed. Most studies conclude that oncology specialists should become more aware of the latest achievements in fertility preservation medicine, should be more sensitive to individual patients' values and goals and should work within a multidisciplinary framework. Kim and colleagues suggest to have a highly skilled team consisting of oncologists, fertility specialists, embryologists, and mental health professionals [58].

Physicians have often prejudices based on patients' socioeconomic background, age, partnership status, existing children, sexual orientation, and in some cases religion. Proper training could provide skills and tools to manage these biases. For instance, oncologists in Saudi Arabia have a favourable attitude towards sperm banking for male patients but referral numbers are still low [46]. In Iran nearly half of the oncologists think that fertility preservation topic should be brought up by patients themselves [56]. It is interesting to note that enthusiasm about fertility preservation options does not generally lead to be better physician-patient relationship [59] which brings us back to the point that survival might still be primarily concern for the majority of oncologists.

Table 3
Physician practices and factors influencing decisions.

Country; publication year	Participants; type of survey	FP consultation practises (%)	Factors influencing decision to/ not to discuss FP (%)	References
UK; 2013	100 oncologists; online	97% usually or always discuss treatment effect on fertility 67% have referred patients to fertility specialist 38% provide written information about fertility	93% patient too ill to delay treatment 88% poor prognosis 72% patient has hormonally sensitive tumour 44% patient already has children 32% patient is single 27% patient could not afford FP 21% patient is homosexual	[53]
UK; 2012	306 surgeons, oncologists, clinical nurse specialists working with breast cancer patients; online	Average number of referrals to fertility unit was 3 patients (range 0–25) per respondent in the last 12 months	78% patients age 37.9% final tumour/node/ metastasis status 37.3% concern that it delay chemotherapy 33.5% whether patient already has children 24.7% whether patient has partner 22.6% oestrogen receptor expression 20.9% lack of knowledge 19.9% concern that FP would compromise the treatment success	[49]
Japan; 2013	434 breast oncologists; paper surveys sent by mail	83% positive in discussing FP 42% refer patients to reproductive specialist when patients express concerns	51% high risk of cancer reoccurrence 45% lack of reproductive specialists 45% time constraints	[57]
Saudi Arabia; 2010	103 medical, radiation and surgical oncologists working with male patients; self administered questionnaire	94% felt that FP help patients psychologically 42% routinely discuss FP with patients 63% positive about discussing FP with parents of prepubertal boys 39% never refer patients to FP specialist 19.5% refer patients to fertility specialist	92% type of cancer 87% patient's age 82% marital status 84% number of existing children 69% cost of sperm cryopreservation 2.9% religion	[46]
Turkey; 2012	25 haematologists; questionnaire	60% did not inform their patients about FP 76% did not feel they have enough knowledge about FP 80% expressed approval of postponing treatment for a short period to accommodate FP	Not provided	[55]
Iran; 2011	30 oncologists; questionnaire	46% knew about FP techniques 40% insisted that patients have to bring FP topic themselves	67% believed FP should be offered to all patients at risk	[56]
USA; 2013	185 hematopoietic cell transplant physicians; online	55% refer to fertility specialist	92% patients were already infertile 63% patients were too ill to delay transplant 35% insurance does not cover FP 33% patients cannot afford to pay FP 27% time constraints 16% no sufficient knowledge 15% do not have information to give to patients about FP 14% patients do not want to discuss FP 12% there is no FP specialist	[60]
USA; 2010	249 oncologists working with female patients; online	95% discuss FP 5.8% always refer to fertility specialist 33.2% usually refer to fertility specialist 43.3% rarely 17.8% never	30% poor prognosis 22% need to initiate therapy in 1–2 weeks 10% patient has a child already 8% poor success of FP 7% patient too young to have children 6% limited knowledge of risks 5% lack of availability of FP services 4% cost is prohibitive 2% patient is a lesbian 1% patient is not married	[54]

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Table 3 (*continued*)

Country; publication year	Participants; type of survey	FP consultation practises (%)	Factors influencing decision to/ not to discuss FP (%)	References
USA; 2009	613 oncologists working with adult patients; postal survey and online survey	46.7% always or often referred patients who had questions about fertility to fertility specialist	Not provided	[61]

Table 4
Skills needed for oncofertility counselling.

Skills	Key features
1. Understanding medical and clinical reality	Disease impact on future life: – What functions will be impaired – What are treatment side effects – What are survival rates – What care will be needed during treatment and after it is finished
2. Informing about fertility preservation options	Established and experimental options: – Local availability – Success rates – Risks and benefits – Costs – Who will cover the costs: public health system, private insurance, charities, private funds
3. Identifying patient's expectations	Personal values and goals in the light of the prognosis: – What treatment is acceptable – What are the tenets of patient's personal philosophy – How much risk (survival versus fertility) patient is ready to accept – How important is fertility, survival, quality of life
4. Legal guidance*	Local, regional, national, federal legislation on fertility preservation methods
5. Psychological and emotional support*	Fear, anxiety, present and anticipated guilt
6. Spiritual and/or religious guidance*	Are there religious preferences? – What FP methods are acceptable – What FP would mean
7. Financial counselling*	Planning finances during cancer treatment: – Reduced capacity to work – Lower income during the course of treatment – Personal care expenses – Cancer treatment expenses not covered by insurance – Childcare (if any) expenses – Fertility preservation (treatment and storage) expenses

* These counselling services could be optional, depending on the need and relevance in a specific situation.

Practicalities to consider in oncofertility consultation

Fertility preservation consultation is an additional concern on top of cancer treatment, but addressing fertility issues in cancer care should become a standard practice (Table 1). Discussing treatment consequences on sexuality and fertility might involve more parties than just patients and physicians. Children have parents to represent their best interests, patients in committed relationships might want to have their partners involved in decision making, some cultures and faiths might find adequate to have other family members, friends and/or religious or community leaders involved. Up to now, the involvement of other parties in fertility preservation decision making has not been investigated. Research focusing on the partners of cancer survivors and their concerns regarding fertility is suggested [40] and EUSOMA guidelines endorse partner's involvement in fertility consultation [37]. Considering the above mentioned concerns, some scholars urge the need to focus on oncofertility implications on both societal and individual levels [62]. Important points to consider when creating functional oncofertility system should include the following: privacy and confidentiality, consent/assent, safety and efficacy of experimental techniques, conflict of interest regarding patient needs and personal/institutional financial incentives, age restrictions (minimum and maximum), future use of stored tissue, gametes, and embryos, creation of centralized registry of those who preserve their fertility [63]. Decision support interventions, like decision counselling or decision coaching, are tools designed to help patients to participate in specific and deliberated decision making among health-related options. They help patients to recognize the values-sensitive nature of the decision and to clarify, either implicitly or explicitly, the value they place on the benefits, harms, and scientific uncertainties [64,65].

Moreover, it is important to keep in mind that the field of fertility preservation in cancer patients, as well as that of infertility treatments, was shaped by medical and non-medical factors such as societal attitudes regarding infertile people, having children as means of survival and work-force or, what is more common in modern society, seeking fulfilment in life [66]. Ethical issues are important aspect of decision-making process. Therefore, we suggest that ethical aspects should be included in decision support interventions.

Financial reimbursement for fertility preservation treatment is one of the most debated questions in the USA [7]. Some argue that there is little ethical justification to withhold insurance coverage for fertility preservation technologies [16] while reservations can still be expressed especially when it comes at tax payers' expense. Various experts have debated on what factors should be targeted to eliminate disparities including socioeconomic status, race, biology, access to care, lack of insurance, stage of the disease at diagnosis [33]. United States had a 14% decrease in mortality from cancer in a period between 1991 and 2004 but it has not benefited to all segments of the population. Thus, ASCO issued a policy statement pointing out that low income, lack of insurance and restricted access to care are playing a major role in health disparities [67]. In

a later report ASCO concluded that providing quality care to all patients with cancer, regardless of their racial, socioeconomic, or geographical group, is a priority [68].

Preserving fertility impose significant costs and in case of cancer patients it is not clear if cryopreserved material will ever be used for the benefit of the patient. Initial oocyte retrieval cost is advertised $6000–12000 plus $2000–5000 for medication (2014-01-31 at Extended Fertility Website http://www.extendfertility.com/about/faq.php), annual storage fee with Extended Fertility in Massachusetts is reported to be $440 [69]. In Germany patients have to cover the costs of fertility preservation themselves: cryopreservation of fertile eggs costs about 3000 Euros, sperm cryopreservation about 350 Euros, storage of either about 250 Euros a year [39]. The cost of fertility treatment led to proposal of guidelines where criteria for experimental gonadal tissue cryopreservation include high risk of future infertility and a high likelihood of long-term survival to avoid medical interventions that can lead to irrational investments [70]. The annual storage fee for cryopreserved materials could easily become a source of psychological pressure and financial burden rather than future opportunity [71].

Therefore we suggest that more attention has to be paid to designing decisional support services for cancer patients. Informing patients, their parents or guardians, on how cancer treatment could affect future fertility in an age, disease and gender specific way is already a standard suggested by many professional guidelines (Table 1). Providing information about fertility preservation options and referring patients for specialist care is also a practice supported by many physicians (Table 3). However, high quality patient care does not end with referral to another specialist. Other types of support have high potential to benefit cancer patients too. We provide more details in Table 4 and suggest that a high quality cancer care should include multiple steps in limited time which will require close and efficient collaboration among a wide range of specialists. Assisting patients to understand the implications of their condition for their future life and choosing fertility preservation options accordingly should be the core part of decisional counselling services. Furthermore, we suggest to focus on patient's values based on their personal philosophy of life, spirituality and emotions ignited by cancer diagnosis. These factors may be integrated with practicalities such as national legislation and financial implications.

Conclusions

In most cases the main cause of infertility in cancer patients is treatment, not the disease. Therefore, consultation for fertility preservation should take place before cancer treatment. The established and experimental methods to preserve fertility are now available in many centres and cancer patients demonstrate interest in fertility preservation. Nonetheless, a significant number of patients worldwide are not given information about the detrimental effects on fertility of cancer treatments and the possibilities to preserve fertility. Physicians are still misled by their personal judgmental biases on whom to offer fertility preservation consultation. Lack of time and knowledge about existing options, poor prognosis, and delay in treatment, patient's age, partnership status, existing children and socioeconomic situation are identified as the main barriers to initiate the consultation. Moreover, fertility preservation consultation is not limited to medical aspects. Patient's needs, values and priorities have to be addressed within the context of medical necessities, realistic survival forecast, socio-cultural environment and availability of resources. We suggest a framework for improving decisional support services for cancer patients who would like to consider fertility preservation options. Our proposal is based on helping patients to clarify the implications of their condition for the future life, identify the values on which their base their personal philosophy of life and address practical aspects of the preferred decision on fertility preservation procedures.

Conflict of interest

The authors do not have any disclosure to make, nor any conflict of interest.

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