

Perceptions and experiences of fertility preservation in Greek female cancer patients

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Abstract

Background

As advances in oncology have led to remarkable and steady improvements in the survival rates of cancer patients and anticancer treatment can cause premature ovarian failure in women, fertility preservation has become a global public health concern and an integral part of the care for women diagnosed with cancer during reproductive age. However, for various reasons, fertility preservation remains underutilized for cancer patients. There are substantial gaps in our knowledge about women's experience and perceptions on the issue. This study aims to contribute to bridging that gap.

Methods

This prospective qualitative study was conducted from March 2018 to February 2023. A combination of purposive and snowball sampling was used. Data were collected by semi-structured interviews with nineteen reproductive-age women with a recent cancer diagnosis. Data were classified and analyzed by a thematic analysis approach.

Results

A variety of distinct themes and subthemes emerged from the analysis of the interview data. The cancer diagnosis emerged as a factor that considerably affects the women's attitudes towards biological parenthood: It can further increase their (strong) previous desire or decrease their previous (weak) desire. Women with a recent cancer diagnosis did not receive adequate and multidisciplinary counselling, including clear and sufficient information. However, participants felt satisfied from the information they received because they either received the information they requested or remained in denial to get informed (i.e. because they felt overwhelmed after the cancer diagnosis). Embryo cryopreservation emerged as a less desirable fertility preservation option for women with cancer. Participants showed respect for human embryos, not always for religious reasons. Surrogacy emerged as the last resort for most participants. Religious, social or financial factors did play a secondary (if any) role in women's decision making about fertility preservation. Finally, male partners' opinions played a secondary role in most participants' decision-making about fertility preservation. If embryo cryopreservation was the selected option, partners would have a say because they were involved with their genetic material.

Conclusions

The findings that emerged from data analysis were partly consistent with prior literature. However, we identified some interesting nuances that are of clinical importance. The results of this study may serve as a starting point for future research.

Introduction

Fertility preservation in cancer patients has become a global public health concern in recent decades. Advances in oncology have led to remarkable and steady improvements in the survival rates of cancer patients [1–3]. ‘Both chemotherapy and irradiation have been demonstrated to damage the ovary and increase the risks of premature ovarian failure (POF), early menopause, ovarian endocrine disorders, and sub- or infertility’ [3]. Fertility preservation is an emerging discipline that has become an integral part of the care of reproductive-age cancer patients due to the rapid progress in reproductive technologies and the high survival rates in young women with cancer. While patients with recent cancer diagnosis have to deal with a devastating and daunting diagnosis, ‘...quality of life (QoL) has been increasingly recognized as an important endpoint’ [4]. Novel oncological treatments such as radio and chemotherapy may cause premature ovarian failure in female patients, thus impairing their reproductive ability [1, 5–7]. However, given the constantly advancing and promising technology, young women with recent cancer diagnoses are often faced with complex decisions involving the complicated concept of Q-o-L. Shreshtha et al. put it best in saying, ‘Although there is an instinctive understanding of the term “quality of life,” there are multiple definitions, which gives testimony to the fact that it is a complex concept with many diverse facets and components’ [4]. Importantly, there are “complex trade-offs and underpinning factors that make patients with cancer choose quality over quantity of life” [4].

It is widely argued in the literature that reproductive capacity in humans is strictly related to autonomy, well-being and quality of life [6–8]. More properly, fertility preservation should be considered an active medical treatment (not simply an intervention aiming to improve the patient’s well-being), especially from the perspective of the holistic-positive definition of the concept of ‘health’. Valle et al. put it best in saying, ‘there is a need to move from a biomedical model of health care to a holistic approach, that is, a shift from a biomedical approach of cancer treatment towards a holistic understanding of the impact of cancer on the individual’s quality of life, taking into account both the physical and the psychosocial dimensions of this experience’ [7]. Fertility preservation in cancer patients (onco-fertility) is a ‘relatively new trend in modern medicine’ [9]. It is an emerging medical area that gives rise to many ethical dilemmas. Fertility preservation involves medical, surgical and laboratory procedures to preserve fertility in people who are at risk of premature loss of their reproductive potential [7, 10–12].

There are various fertility preservation methods that are currently applied in the field of onco-fertility. The following quote describes properly the options that are currently available: ‘Currently, for adults and post-pubertal girls, oocyte or embryo cryopreservation is an established method. If their cancer treatment cannot be postponed for 2 weeks, ovarian tissue cryopreservation is offered as an experimental technique’ [11].

However, fertility preservation remains underutilized for various reasons. To date, the literature highlights that women with cancer during reproductive age are often provided with inadequate information about the available fertility preservation options. In a study published in 2015, Waimey et al. stated, ‘many primary care physicians lack the awareness and exposure to current clinical literature on the reproductive

impacts of cancer treatment' [13]. In the conclusion section, the authors recommended 'early referral to either a reproductive endocrinology and infertility specialist or a gynecologist comfortable with discussing fertility preservation options' [13]. Much more recently, Brown et al. state, 'Despite this, research has shown a lack of knowledge and uniformity in how health care professionals (HCPs) manage fertility preservation (FP) discussions in young women with breast cancer and show that women have unmet needs regarding FP' [14]. The authors concluded that 'There is a need to provide adequate resources and education to HCPs for the provision of standardized care' [14]. Del-Pozo-Lérida et al. conducted a literature review and found that '...despite the growing advances in the subject, optimal counselling from healthcare professionals should always be present' [1].

Ultimately and most importantly, according to the literature, there are substantial gaps in our knowledge about cancer patients' experiences [15, 16]. More specifically, there is a substantial gap in our knowledge about cancer patients' specific feelings or needs for fertility preservation options [15, 17]. This study aims to contribute to bridging that gap.

Study design

The present work was a prospective qualitative research study based on in-depth interviews conducted with female cancer patients of reproductive age with a recent diagnosis of cancer who are considering or have considered fertility preservation as a means of overcoming the risk of cancer treatment-induced infertility. This qualitative descriptive study was conducted from March 2018 to February 2023. Participants' recruitment and data collection took a long time because of the COVID-19 pandemic. Thematic analysis was used as the methodological orientation of the study.

Inclusion criteria

This study included a) women of reproductive age with a diagnosis of primary cancer who b) were able and willing to reproduce. Furthermore, interviews should be carried out prior to or during chemotherapy treatment.

Exclusion criteria

Women who a) were not able to perform fertility preservation discussions at the time of interview as well as b) women with bilateral ovarian cancer were excluded from the sample of this study.

Materials and methods

In-depth individual semi-structured face-to-face interviews were conducted after approval through the Ethics and Deontology Committee of the Medical School of the Aristotle University of Thessaloniki (Reference number: 3.663/2.5.2018) and the Scientific Committee of the "Papageorgiou" Hospital of Thessaloniki (reference number: 297/14-05-2018). A purposive sampling method was used to reach possible participants. To enhance the diversity of the sample, participants were recruited using a

multimodal recruitment technique. Participants were recruited from the Oncology department of one large University teaching hospital of Thessaloniki ("Papageorgiou" Hospital), interviewer's (A-MT) personal acquaintances, and referrals made from physicians with different specialties who are involved in the care of young women with cancer or their fertility preservation (oncologists, breast surgeons and fertility healthcare professionals). Furthermore, researchers used the snowball sampling technique to recruit participants using a small pool of initial participants as informants. Possible participants were contacted face-to-face to be given information and then confirm participation and find a suitable time and place for carrying out phenomenological interviews.

The interview guide was developed prior to conducting interviews and reviewed by a bioethicist with experience in reproductive ethics (PV) and a qualitative researcher (A-MT). Semi-structured questions were developed on the basis of the results of a review that was initially conducted on the literature on the topic of interest. It was slightly refined after the initial results from a few interviews to make the interview guide more probing. Questions mostly focused on women's understanding of biological motherhood and fertility preservation, how they were given information on this, how they felt about doing it, and what were the influences behind decisions of participants considering fertility preservation. The interview guide included questions such as 'What is it like for you to be a child's biological mother?' (*a grand tour question to make the participant comfortable*), 'What is your understanding of fertility preservation as a means of overcoming the risk of cancer treatment-induced infertility?', 'How did you experience considering fertility preservation as a means of overcoming the risk of cancer treatment-induced infertility?' 'What were the influences behind decisions made by you considering fertility preservation?' 'How satisfied are you with the information you were given on this topic, and why?', 'How easy did you find discussing fertility preservation with physicians or other health professionals?'. As the questions were semistructured, they included questions such as 'when you were diagnosed with cancer, had you completed your desired family size [had you as many children as you hoped to have]?' and 'after diagnosis, but before you started treatment, did you see a fertility specialist to talk about fertility preservation?'

Data collection ceased only when data saturation was reached. Field notes were taken immediately after each interview and were taken into account by researchers when conducting data analysis. Validity was observed by using maximum variance in participant selection. Reflexive thinking was employed throughout the research process to reduce unintentional personal bias and enhance the trustworthiness of the study. The participants did not provide feedback on the findings.

The interviews were conducted at interviewees' preferred times in quiet and neutral places of their choice with only the interviewer (A-MT) and participant present. The interviews were audio-recorded and then transcribed verbatim. After carefully reading and rereading each interview transcript, the researchers coded units that were similar in meaning. Codes with similar meanings were grouped into subcategories. Then, subcategories were condensed into categories, which in turn were grouped into themes. Disagreements among the authors were addressed through discussion. The research was conducted by a

multidisciplinary research panel including bioethicists, lawyers, oncologists and obstetrician-gynecologists specialized in human reproduction.

Results

The participant characteristics are presented analytically in Table 1.

Table 1
Participant characteristics.

Participant	Age	Type of Cancer	Children
P1	30	Breast Cancer	0
P2	40	Cervical cancer	0
P3	33	Breast Cancer	0
P4	36	Breast Cancer	2
P5	35	Breast Cancer	1
P6	40	Breast Cancer	1
P7	35	Breast Cancer	1
P8	44	Breast Cancer	1
P9	35	Cervical cancer	0
P10	35	Breast Cancer	0
P11	32	Breast Cancer	0
P12	31	Colon cancer	0
P13	45	Breast cancer	2
P14	43	Breast cancer	0
P15	18	Ovarian Cancer	0
P16	43	Stomach Cancer	0
P17	31	Breast cancer	0
P18	38	Lymphoma	0
P19	36	Breast cancer	0

The thematic data analysis revealed five major themes and eight subthemes (Table 2).

Table 2
Major themes and subthemes.

Theme	Subtheme
1. Many patients had a strong and deeply held desire for biological offspring.	<p>1.1. Facial resemblance and similarities of offspring to mother and a good relationship with spouse /partner emerged as reasons behind the desire for biological offspring.</p> <p>1.2. Cancer diagnosis can make clear and strengthen the women's desire to reproduce.</p> <p>1.3. Cancer diagnosis can clarify and strengthen the women's desire to reproduce.</p>
2. Patients preferred oocyte cryopreservation to other fertility preservation options.	<p>2. 1. Unwillingness to preserve embryos by cryopreservation for different reasons.</p> <p>2. 2.Surrogacy for fertility preservation emerged as ultimum refugium option.</p> <p>3. 1. Lack of clear information.</p>
3. Provided information was unclear and deficient.	<p>3. 2. Deficient information.</p> <p>3.3. Satisfactory information was only provided after patient questions.</p>
4. Patients decided for themselves. They made decisions together with their husbands/partners for some specific reasons.	
5. Religious, social and financial reasons did not emerge as factors affecting participants' fertility preservation decisions.	

Table 2. Major themes and subthemes.

Many patients had a strong and deeply held desire for biological offspring.

Facial resemblance and similarities of offspring to mother and a good relationship with spouse/partner emerged as reasons behind the desire for biological offspring.

Data analysis concluded that, with few exceptions, most participants had a strong deeply held desire for biological offspring. Participants said that their desire for biological offspring reflects a woman's desire to create a human being, that is, her future self-continuity of herself, having similar traits and looking like she.

P9 said,

...having biological offspring is very important. It is like continuing yourself. It is fascinating to know what your child will look like, whether or not they look like you, what traits of yours they will have.

In a similar vein, P1 said,

"I find it charming to see someone like myself grow up, mainly as evolution of myself ..."

Furthermore, participants said that their desire for biological offspring depends on the existence of an appropriate partner. P2 said,

... to me, becoming a parent is directly connected to companionship. The right partner and chemistry within the couple at the time of becoming parents are very important. I have always wanted someone to be co-responsible...

Similarly, P3 said,

"after [cancer] diagnosis I would possibly think about an offspring only in relation to a partner"

Participant P19 said,

"...having a child results from the bond between yourself to your partner"

One participant said that she desires to have a biological offspring because it is *"something very beautiful"* (P6), with another participant saying,

"I need to experience pregnancy" (P2).

Remarkably, none of the participants considered having a biological child as the only solution.

Cancer diagnosis can weaken women's desire to reproduce.

Some participants stated that it was not very important for them to become mothers. However, while they had clearly expressed their previous desire to have biological offspring, they reported a range of cancer diagnosis-related reasons weakening their original desire for biological offspring. Perhaps their original desire was not strong enough. One reason was the fact that these participants were not nulliparous before the cancer diagnosis. P13 (46 years old, who already had two children at the time of diagnosis and was interested in having a third child) said that if she had not a child already, having been diagnosed with cancer, she would think of preserving fertility even if she had to postpone cancer treatment. However, if chemotherapy had to start *"so immediately"*, then her priority would be fighting the disease. The participant's voice emphasized the term *"so immediately"*. In a similar vein were other participants who had already had a child at the time of diagnosis. Furthermore, among the cancer diagnosis-related reasons reported (in many cases cumulatively) as weakening their original desire for biological offspring were woman's quality of life that might have been negatively impacted in case of distressing recurrent failure in assisted reproduction (P1, P10) or from negative consequences of fertility preservation methods

(P2) and at any rate from the oncological disease itself. A mother's low quality of life negatively impacts the quality of life of the future offspring. An ill mother would be unable to meet her parental duties (P9, P1, P12, P5, P6). For instance, Participant 6 said,

"I would not take the risk to leave a child without his or her mother, wittingly, while I know my disease." (P6).

Furthermore, participants expressed their fear that cancer itself can be passed down from parents to children (P6, P10, P19). Other reasons weakening participants' desire to reproduce were the patient's disorientation from fighting her disease (P2) and lack of partner. Participant 2 said, *"I have always wanted someone to be co-responsible..."*. Moreover, participants emphasized the patient's advanced reproductive age, given that in all likelihood she would undergo assisted reproduction many years later due to anticancer treatment (P2). Finally, among the reasons weakening the desire to preserve fertility were reported financial reasons, which were always reported cumulatively with other reasons (P14, P2, P18, P7, P11).

Finally, it is to be added that some participants said they felt compromised with the idea of childlessness and let themselves go with the course of the events given the threat of cancer (P15, P16, P18).

Cancer diagnosis can clarify and strengthen women's desire to reproduce.

Cancer diagnosis may act as the two sides of the same coin. It not only can weaken the desire for biological offspring but also might make it stronger.

Another category of participants included those with a very strong (deeply held) original desire to reproduce, so that they made clear at the beginning of the interview that they would not recede even if their life was threatened. Note, however, that later in the course of the interview, they said they would only recede in case of extremely high risk for their life or child's well-being.

Participant 12 said,

When I was informed about [possible infertility and] fertility preservation I cried a lot. Note, however, that when I heard about cancer diagnosis I didn't! !

The participant would rather give priority to fertility in case of disease-fertility conflict. She said it was very important for her to bear a child, although the cancer she suffered was aggressive.

Interestingly, Participant 11 stressed,

"After cancer diagnosis, the first thing I thought of was my fertility rather than if I shall live or not" and that *"the procedure of preserving fertility was not carried out in a good mood and this bothered me psychologically more than the very procedure of fighting cancer"*. However, she pointed out both the challenge she was experiencing while fighting cancer and her respect for the moral status of the human

embryo, which might eventually be destroyed because it might be redundant, as important obstacles to preserving fertility.

Furthermore, cancer diagnosis can clarify the internal attitude of female cancer patients towards having biological offspring because it brings them face-to-face with the dilemma of preserving fertility or not, a condition/question in which the patient has to come to a decision immediately. Although participant 3 did not want to have children before diagnosis, she said,

"...lack of the possibility to choose changed my mind... I would like to have the option." Participant 2 was in a similar vein. While Participant 1 was previously at a loss to make a reproductive choice, after cancer diagnosis, she turned out to be clearly positive towards having a child.

Patients preferred oocyte cryopreservation to other fertility preservation options.

Some participants were reluctant to opt for embryo cryopreservation due to religious or nonreligious reasons. Furthermore, almost all participants expressed more or less strong concerns about surrogacy as a fertility preservation option for various reasons.

Unwillingness to preserve embryos by cryopreservation for different reasons

Some participants clearly expressed their unwillingness to opt for embryo cryopreservation for were reluctant to opt for embryo cryopreservation, showing respect for the moral status of the early human embryo on a religious or not basis or because of having received inadequate information about the particular fertility preservation method.

Participant 16 declared her reluctance to opt for embryo cryopreservation, absolutely for religious reasons. She said,

"I believe in God and feel that the fertilized oocyte is an early existence of man...oocyte is something that goes to waste every month, it is not the same to fertilized oocyte".

She noted that she would not want to throw away any embryo; for this reason, she would make as many efforts as the number of fertilized oocytes.

Participant 9 said that she would not proceed with the cryopreservation of embryos for religious reasons without providing any further detail.

Participant 11 was a hundred percent against cryopreservation of embryos because of her increased respect for early embryo moral status, which was not related to religiosity or spirituality. She said,

I feel that I create embryos, some of which will be used (to achieve pregnancy), with the other embryos being thrown away. I do not accept it for moral reasons.

Participant 17 would not proceed with embryo cryopreservation not because of moral reasons but due to a lack of adequate information she had received. She said,

"I think I would not do it, it is something unfamiliar to me... not because of ethical concerns... maybe I have not yet received needed information ..."

Participant 19 said she would not opt for embryo cryopreservation, not for moral reasons but because she was of the view that having an offspring is strictly related to the existence of partnership. She did not know if they would be together in the future. She said,

I did not proceed to embryo cryopreservation not because I am morally committed, but because I do not know what will be the relationship status with my partner after I will have gone through all this [the disease] ... I would not like to be committed to something that would affect future decisions regarding having offspring.

Among participants in this study, respect for the human embryo's moral status is discussed as a barrier to fertility preservation and has emerged as a major barrier to opting for embryo cryopreservation.

Surrogacy for fertility preservation emerged as an ultimatum refugium option

All participants expressed more or less strong concerns about the use of surrogacy as a fertility preservation option for various reasons.

Participants said that they could resort to surrogate uterus only with persons closely related to them. Otherwise, moral precautions rise since surrogate uterus is exploitation of a foreign female body, as well as trust matters. P11 said,

"Surrogacy would be one of my last choices... I cannot pay a woman to give me a part of her body"

Participant 12 said that surrogacy is a method that,

I would not opt for, because it hurts the woman that gives birth, even if the offspring is not hers [genetically].

However, the participant has made discussions with her sister to become a surrogate for her [the participant]. Participant 13 said that she would not enter into the process of surrogacy because *"as a human, it does not seem to be ethically correct to me ..."* Participant 9 said that surrogacy is something that looks unfamiliar to her. However, she said that she might opt for it under certain circumstances, for instance if the surrogate mother is *"a woman being in a very close relation to me, mother or other relative...this could make me opt for it [surrogacy]."*

Participant 13 said,

Surrogate motherhood makes me feel strange, nevertheless if I could not have the option to have an offspring, I would try to find the proper woman to get pregnant for me, maybe a woman with whom I have an intimate relationship, like a sister, mother, a person that is very close to me...

Other participants considered surrogacy *to be the ultimate refugium* (P14 P17, P18). Two participants expressed a strong negative attitude towards opting for surrogacy as a fertility preservation method. Note, however, that these participants already had children and did not feel a strong desire for having other biological offspring (P5, P6).

Provided information was unclear and deficient

Lack of clear information

This emerged as a highly recurring finding within data analysis. Participants reported that the information they were given about their fertility preservation was not clear. A diffusion of responsibility for providing information about fertility preservation was identified between oncologists, surgeons and fertility specialists, who sometimes had different opinions.

Participant 19 said,

As to [the side effects of] ovarian stimulation during the procedure of fertility preservation, I not receive a clear answer. This made me feel involved in a precarious situation because I would not like to do something that could harm my health. Furthermore, I did not know how harmful it could be, how to evaluate my priorities.

In a similar vein, Participant 11 reported controversial views between physicians (oncologist, surgeon and fertility specialist).

Participant 9 said,

"I wish I had received more clear information.... I felt that there were questions regarding many aspects of fertility preservation, which were not clearly answered by physicians." She added,

I want [the physician] to admit that a clear and accurate answer on this subject is lacking yet... I need a well-informed physician to become a well-informed patient.

While Participant 1 declared she felt satisfied with the information she was given, she added,

...fertility preservation is a grey zone ... they neither said to me it is permitted nor it is prohibited... in clarity...

While different medical specialties are involved in the field of onco-fertility, the vagueness of provided information may be due to physicians' unwillingness (irrespective of their specialty) to take full responsibility for the information provided to a patient.

While the oncologist allowed Participant 14 to proceed with fertility preservation,

“...at that time, he realized for the first time that he had not mentioned the subject of fertility preservation at all, he justified himself saying that he believed information was given to me by the surgeon. The surgeon considered that I was informed by the oncologist and, in this way, I had never been informed for the possibility to opt for fertility preservation”.

Deficient information

A good number of participants said that the information they received was deficient and that they were not satisfied with the process within which information was provided to them. This emerged from data analysis as a recurrent finding. The following quotations are representative to illustrate this point.

Participant 2 said that she was not satisfied with the information she had received, and she noticed,

I consider that if the excellent degree is 10, I would give 3.5. I wish the medical specialists' group were provided with an in-depth and overall view [of what they had to inform me about], from the time of diagnosis...

In a similar vein, Participant 14 said that no physician informed her about fertility preservation, although she had no children and wanted to have one. She contacted a fertility gynecologist, and the procedure of preserving fertility was immediately on the way, without being further informed.

Similarly, Participant 11 said,

...the way the fertility physician communicated with me was not a decent one. It was cold, absolute, pressing. He made me anxious and said I had to give an answer 'at the soonest possible time'... he did not give me even a single day to think.

Satisfactory information was only provided after patient questions.

Many participants considered that they were given adequate information and declared that they were satisfied with it. However, they noted that the information they were given (perceived as adequate) was received after having asked physicians to provide them with further information about specific aspects of fertility preservation options. The following quotation is representative of this point.

Participant 19 said,

...my physicians 'informed' me. In general. However, I am satisfied with the information I finally got. I received answers to most of my questions because I had asked these questions. I do not know if I would have been given adequate information as well, if I was less 'pressing'...

Furthermore, some participants were satisfied with the information they received because they wittingly avoided asking further questions to the physicians (though they could) for various reasons. Participants preferred to trust their physician and avoid taking responsibility for fertility preservation decisions. This was a highly recurring finding. While Participant 3 declared she felt satisfied with the information given, she said she had not asked questions because she thought she knew all she needed to know. She was certain that hormone therapy would negatively influence her cancer. Her top priority was to overcome her oncological disease as soon as possible. In a similar vein, Participant 4 declared satisfaction from the information she was given, but she admitted she had not asked much because she already had a and did not need to learn more.

Furthermore, Participant 5 was satisfied with the information she received from her physicians. She said, I could have asked for more information...[however] because of the “shock” I experienced when I was informed about diagnosis, I could not ask for more ...

Moreover, Participant 6 said,

...the information I received from physicians was ok, it encompassed all I needed to know...

In the same vein, Participant 12 learned about the possibility of preserving fertility from a person who was not a physician! Finally, however, she felt satisfied with the information she received and said,

The information provided encompassed all I needed to know...I did not want to know anything else. I felt satisfied. My only complaint was that the communication should be more polite.

Similarly, Participant 13 said,

“I learned what I had to learn”.

In the same vein was P15.

Participant 16 said,

I wanted to be offered a treatment, which I had no choice but to accept ...I would have liked not to have to make a [difficult] decision. I wanted to feel that I trust my physician...

In a similar vein, Participant 7 said that she trusted her physician. She said,

I did not ask much.

Four participants (P1, P14, P17 and P8) declared that they were not satisfied with the information they received. Note, however, that two of them (P14 and P8) stressed that they had avoided asking questions to physicians for various reasons.

While Participant 17 was reluctant to receive further information, she considered the given information very deficient in the area of fertility preservation. The participant said,

I as a patient I did not wish extremely much information because I felt overwhelmed so that I could not function. I said no, I do not want to know so much [information]...

Furthermore, the participant complained “...no physician informed me about the risk of cancer activation by hormones provided within the fertility preservation process...”

Furthermore, Participant 8 did not ask questions of the physicians because she did not trust them enough.

Finally, in some cases, physicians may wittingly avoid providing fertility preservation information to patients due to their belief that there is no point to do this given that the chemotherapy could not be postponed (P18).

From data analysis, it emerged that physicians may avoid providing information about the available fertility preservation options for the following reasons: a) The patient is not at an advanced reproductive age, and the possibility of having a future offspring is very high (P15 18 years old, P1 30 years old). b) Physicians must hurry to initiate anticancer therapy as soon as possible, and there is no time to lose (P18). c) The patient already has one offspring (P13, P4). d) The type of cancer is hormone-sensitive cancer, and the available fertility preservation method involves the administration of hormones.

Participants P1, P2, and P3 said that their physicians said they would not suggest fertility preservation. In the same vein, Participant 9 said, “My physicians informed me that I had better avoided proceeding with fertility preservation”. In a similar vein, Participant 11 said, “... my surgeon had a negative attitude towards proceeding with fertility preservation before surgery.” e) The patient is not interested in proceeding with fertility preservation (P3, P6, P2). For instance, Participant 2 said, “Though my physician advised me to make a referral to a fertility specialist, I decided not to do this... While I had an appointment with a fertility specialist, I have never been there...”

Patients decided for themselves. They made decisions together with their husbands/partners for specific reasons.

Most patients had finally decided for themselves if they would apply for preservation of fertility methods. Husbands' / partners' opinions were simply taken into account. The same holds for their family or friends. However, if husbands/partners had (or would be) participated with their own genetic material, as in the case of embryo cryopreservation, their opinion was seriously taken into consideration in women's fertility preservation decision-making process. Two participants pointed out that the husband/partner plays a pivotal role in preserving fertility if he has offered his own genetic material, as in the case of embryo cryopreservation. Participant 9 said,

The partner plays a very important role if the child that will be born also has his genetic material; however, since fertility preservation is an invasive procedure regarding the woman's body, finally I would make a

decision on my own concerning how to proceed, bearing in mind his opinion.

In the same vein was Participant 10. Additionally, financial reasons might make the husband/partner play a decisive role. Participant 4 said that the decision to proceed to fertility preservation is not a decision that would be made for herself alone but jointly with her husband/partner since the cost of fertility preservation is great.

Participants gave the impression that their trust in an intimate person plays a significant role in decision making. Participant 6 was a pharmacist and said she trusted her husband/partner opinion because he was also a pharmacist.

For almost all participants, parents did not play a crucial role, with the exception of Participant 9, who trusted them because they *"know her well"*. The parents of Participant 15 (a very young woman) decided jointly with the physician, whom they absolutely trusted. She also trusted her physician too much. She said, *"if he had something to tell me he would have said it to me"*.

Religious, social and financial reasons did not emerge as factors affecting participants' fertility preservation decisions.

All participants except for two (P16 and P9) did not report religious barriers to proceeding with fertility preservation. Importantly, the same holds true for participants who described themselves as religious or spiritual. P16 said, *"I believe that this is not a matter that my spiritual leader [confessor] can solve."* Financial factors were always taken into consideration for decision making, without being a determinant factor affecting the participants' final decision. Some participants mentioned financial factors only in addition to other reasons supporting their decision not to apply for fertility preservation (P2, P7, P11). None of the participants reported financial factors as an exclusive reason for not proceeding with fertility preservation. Participants always referred to financial factors (highlighting them to a greater or lesser extent) in addition to other reasons. Finally, none of the participants considered social reasons as factors of particular significance.

Discussion

As assisted reproduction is further developing in Greece, relevant services become accessible for larger parts of the Greek population. However, at present, there are no official data regarding patients who are performing fertility preservation procedures prior to cancer treatments. This research aimed to identify the needs of patients together with gaps in health services and hopefully assist further improvements in the management of premenopausal women diagnosed with cancer.

While most of the participants in this study suffered from breast cancer, six out of nineteen participants suffered from cancer primarily located in other organs: cervical (two participants), ovarian, stomach, colon, and lymphoma. 'The incidence of colorectal cancer among premenopausal women is increasing' [18]. The diversity of cancer types in our small sample is in line with the available literature. Importantly,

despite the huge need of premenopausal women with cancer for fertility preservation prior to treatment, only a small percentage of these patients actually managed to do so.

Participants in this study experienced a lack of close collaboration among all relevant stakeholders involved in their fertility preservation decision. That situation goes against the promotion of the patient's autonomy and well-being. As onco-fertility is an emerging and multidisciplinary field [3], the produced international or national guidelines should be multidisciplinary [19, 20]. Fertility preservation guidelines have been implemented since 2013. In 2020, the European Society of Human Reproduction and Embryology (ESHRE) published a detailed guideline 'written by a multidisciplinary group with gynecologists and fertility specialists, oncologists, a psychologist, a bioethicist, an embryologist, a scientist, and patient representatives' [19]. The same goes for other guidelines developed in the US, Spain or France [20–23].

Comprehensive fertility counselling and optimal care should be provided by a multidisciplinary team of health providers, including 'oncologists, reproductive endocrinologists, mental health counsellors and clinical researchers' [24]. Addressing the need for fertility preservation requires a close and strong collaborative effort of all relevant stakeholders [3, 19, 20, 24–27].

Furthermore, the appropriate fertility preservation method in a given case must follow multidisciplinary strategies. It must be carefully selected upon shared decision-making, involving discussion of potential risks and benefits of the available options, in consensus with all the involved stakeholders [19, 28, 29]. The selection of the most appropriate option should be individualized and may be determined by factors such as patient age, patient characteristics, desire for conception, disease, treatment plan and socioeconomic status [20, 26]. Fertility preservation decision-making in women with cancer is a complex process [30].

Many participants in this study felt that they had received inadequate information. However, some participants felt that they had been adequately informed on their own initiative. These participants were classified into two categories: those who declined further information and those who sought more information and asked further questions to health providers. That is, health providers would only give enough information on the patient's request.

As chemotherapy, radiotherapy or their combination are a great threat to fertility among women with cancer, 'it is...essential that oncologists and hematologists provide adequate information about the risk of infertility and the possibilities for its preservation before starting treatment' [20]. The American Society of Clinical Oncology [21] and the European Society of Human Reproduction and Embryology [19] suggested that healthcare professionals should inform reproductively active women with cancer about the feasibility of preserving fertility as early as possible prior to the initiation of anticancer treatment.

Many authors share that consideration and strongly highlight that the provision of information about fertility preservation in cancer patients is strongly indicated and beneficial to them: it protects their mental health and promotes their quality of life, enables patients to better cope with their cancer-related stress,

can 'boost their confidence in treatment', 'reduces their long-term regret or disappointment concerning fertility', and facilitates patients in making well-informed decisions on their cancer care [3, 20, 22, 23, 27, 30, 31]. It is argued that it is physicians' (particularly oncologists and reproductive endocrinologists') responsibility and moral obligation to address 'fertility preservation options with all reproductively -active women prior to any cancer therapy' [3, 19, 21, 22]. The information provided should be optimized and tailored to the needs of the various subgroups of women [32]. In the context of onco-fertility, the provision of information should be combined with 'appropriate and effective fertility-related' psychological support (fertility counselling) [27]. Nevertheless, onco-fertility counselling is 'under-utilized' for female patients for various reasons [3, 11, 25, 29, 33–35]. Indeed, 'only a small part of young cancer patients received fertility preservation services' [11]. A retrospective study has shown that 'of all the 918 surveyed cancer survivors who had potential reproductively toxic cancer treatments, 61% of them were counseled by an oncologist about their infertility risk, but only 5% of them visited a fertility specialist and 4% of them ultimately chose to preserve their fertility' [3]. Ojo et al. state that in a study... 'half of the young women with cancer in a study received no information from oncologic health care providers about their cancer diagnosis and fertility, and many more received no referral for fertility preservation services' for a variety of reasons [25]. It is argued in the literature that while '66–100% of patients with cancer expressed a need for fertility information', 'about half of patients (43–62%) felt that relevant information was provided inadequately and that their information needs were not addressed' [36]. Suboptimal counselling is a factor that serves as a critical barrier to fertility preservation. This emerged as a recurring finding in the literature review. It is argued that this is due to 'lack of adequate provision of information on fertility preservation and the lack of referral from oncology to the fertility clinic' [11]. Furthermore, it should be noted that the volume and content of fertility preservation information that should be provided to reproductively active women with cancer are not clear and commonly accepted. Importantly, the ESHRE provided detailed guidelines for the content of the fertility preservation information that should be provided to reproductively active women with cancer [19].

Most participants in this study had not received a referral for fertility preservation options. Although women with cancer may be focused initially on their diagnosis, to maintain all the currently available fertility preservation options and increase the likelihood of future child-bearing potential, reproductively active women with cancer diagnosis should be promptly referred to reproductive specialists or psychosocial providers (if necessary) before treatment initiation [22, 29, 30, 37].

In this study, data analysis implicates physicians' lack of knowledge about cancer-related fertility preservation. Health providers should be updated and prepared to discuss fertility preservation options with their female patients facing a new cancer diagnosis and/or to refer them properly as soon as possible [22, 25, 34]. 'The level of knowledge of fertility preservation by oncology care providers has a significant impact on patient education and the subsequent choices they make' [25].

All participants in this study were offered narrow fertility preservation options, mostly oocyte and embryo cryopreservation. Selection of the appropriate fertility preservation option for a particular patient includes a variety of factors such as 'gender, pubertal status, relationship status, religious or cultural beliefs or

available funds to cover fertility treatment; also, disease characteristics such as prognosis, stage, and time-frame for oncological treatment, clinician factors such as knowledge of referral pathways, guidelines, confidence and expertise in managing fertility; and factors such as treatment type and risk of inducing infertility, referral pathways, timely referral, availability of services, and out-of-pocket expenses' [27].

In this study, physicians remained concerned about the safety of controlled ovarian stimulation (COS) for fertility preservation before initiating anticancer treatment, particularly in patients with hormone-sensitive cancer. However, it seems to be due to their lack of experience in communicating state-of-the-art knowledge. While fertility preservation provided before starting cancer treatment can significantly delay cancer treatment initiation, it is argued that 'FP treatments have not been associated with increased recurrence or mortality' [38]. In Sweden, studies that used population-based registers have shown the safety of fertility preservation procedures in women with breast cancer [39].

It is true that the safety of fertility preservation treatments in cancer patients is a matter of paramount importance. However, Arecco et al. conducted a systematic review and meta-analysis and concluded that 'performing COS before, or ART following anticancer treatment in young women with breast cancer does not seem to be associated with detrimental prognostic effect in terms of breast cancer recurrence, mortality or event-free survival (EFS)' [10]. Furthermore, Rodgers et al. in 2017 showed that women with breast cancer can effectively undergo COH for fertility preservation without worsening their prognosis [40].

Almost all of the participants in this study were not provided with information about OTC as a fertility preservation option for select patients. Oocyte and embryo cryopreservation are widely available, long- and well-established preservation options that are most effective for reproductively active women with cancer [3, 19, 21, 22, 30, 41]. 'Embryo cryopreservation has slightly higher success than oocyte cryopreservation in achieving pregnancy' [42]. Embryo cryopreservation is considered 'the most widely available option', which requires the existence of a partner or the woman's openness to sperm donation [25, 30]. While embryo cryopreservation is a long-established and preferred fertility preservation option, the fact that the embryos would be the joint property of the couple can give rise to difficult questions such as who gets the frozen embryo if the relationship ends [19, 30].

Ovarian tissue cryopreservation, in vitro oocyte maturation, ovarian transposition, ovarian suppression, and adjuvant therapy are included among the experimental fertility preservation options for these patients [3, 19]. Ovarian tissue cryopreservation seems to be the front-runner among the experimental options and is on the verge of becoming a well-established fertility preservation option [41, 42]. The technique of ovarian tissue cryopreservation that has recently become available has provided a further substantial expansion to the field of fertility care [31]. Rives et al. state, 'Ovarian tissue preservation is indicated in case of very high risk of infertility' [23]. Henry et al. argue that cryopreservation of ovarian tissue is considered 'a secure tool in human fertility preservation' [43]. While ovarian tissue cryopreservation remains an experimental fertility preservation option, it can be an option for specific

patients [18, 19, 22, 42]. For instance, ESHRE et al. acknowledge that ovarian tissue cryopreservation might be an option in cases of insufficient time for ovarian stimulation or even at patient preference [19]. Importantly, ovarian tissue can restore ovarian function and does not require prior ovarian stimulation [22, 42].

Furthermore, *In vitro* oocyte maturation (IVM) can also be considered, and in some cases, there may be a possibility of combining different approaches' [19]. In Sweden, gonadal tissue cryopreservation is an option available at many reproductive healthcare centers [39].

Cancer diagnosis enhanced participants' desire for biological offspring (especially in participants with a strong desire for children at the time of diagnosis). However, in other patients, cancer diagnosis reduced their desire for biological offspring for various reasons reported by participants (especially those with a weak previous desire for children). Unfulfilled desire for biological offspring can be associated with impaired mental health [27]. To this effect, it is not surprising that young women's desire for biological parenthood seems to remain strong after cancer diagnosis or even after cancer treatment, especially in patients who are nulliparous at the time of diagnosis [28]. Follow-up studies have shown that women who have future child wishes at the time of initial cancer treatment are more open to seeking and receiving fertility preservation consultations [25]. Surprisingly, it is argued that 'It would be wrong to assume cancer patients with advanced disease...have no desire to preserve their fertility' [25].

Financial issues emerged as a fairly important factor affecting fertility preservation decisions. Financial issues must be involved in shared decision making in the context of onco-fertility [22]. Patients with cancer should be made aware of the available financial assistance programs to become more flexible in addressing 'this complex and heterogeneous landscape' [22] 'during an uncertain and challenging time in their lives' [34]. Wan et al. concluded that a 'lack of knowledge, the urgency of cancer treatment, and financial constraints are causes for a low access rate regarding' fertility preservation in young breast cancer patients [44]. Omesi et al. conducted a study and found that in the US, 'utilization of financial assistance for FP was low despite literature pointing to the need for such assistance' and that state-specific insurance coverage began to expand [45]. However, that expansion is not yet adequate. The actual cost of fertility preservation reflects 'how costly the general health care services in that country are' [25]. The US is a country 'where adults with a history of cancer report higher out-of-pocket medical spending' [46]. The use of fertility services may increase the financial hardship among cancer patients in countries where cancer-related fertility preservation services are neither covered by insurance nor otherwise subsidized [25]. It is argued that in the US, better insurance coverage could facilitate access to fertility preservation services and ultimately 'improve long-term cancer survivorship' [46].

Notwithstanding, there are countries where these services are totally or partly subsidized. 'In Sweden... fertility preservation is offered within the publicly financed healthcare to patients when medically indicated' [39]. Furthermore, 'From 2022, health insurance companies in the Czech Republic partially cover the expenses for fertility preservation treatment for cancer patients' [9]. However, as assisted reproduction services are too expensive in many countries, many women with cancer have no access to

fertility preservation services not only in low- or middle-income countries but also in high-income countries [25].

In this study, religious belief emerged from data analysis as a slightly important or not at all important factor affecting fertility preservation decisions. The different religions vary considerably in their attitudes and beliefs on the morality of artificial reproduction. 'While most forms of artificial reproduction are acceptable in Hinduism and Buddhism, its acceptance in Christianity and Islam is variable depending on the branches or sects within the religious group. For instance, all forms of assisted reproductive techniques are unacceptable in Roman Catholicism, while acceptance is variable among Orthodox Christians [25].

Religious beliefs are included among the factors influencing the patient's decision on which preservation options may be available to them [27]. Women with cancer may have religious or ethical objections to embryo cryopreservation [22].

The barriers to fertility preservation utilization in female cancer patients are multifactorial, including patient factors (age, relationship status, desire to have children, disease stage and prognosis, financial capacity), health care provider-related factors (level of knowledge, physicians' belief that the success rate of fertility preservation procedures is low, implicit bias, sense of responsibility, time pressure), socioeconomic factors (cultural views and normative values, religious belief and insurance coverage) and institutional factors (availability of facilities, institutional guidelines and policies) [25]. Ulrich et al. state, 'cost and access to care remain critical barriers to fertility preservation services' [34]. Tomilová and Frühaufová argue that 'lack of information for both patients and, unfortunately, professionals' and 'the high cost of treatment' are critical barriers to fertility preservation services [9]. Furthermore, for women with a cancer diagnosis, selecting to accept fertility preservation is a complex emotional process of making 'one of the most difficult decisions ever made' [27]. As the distress of making a fertility decision is further complicated by the concurrent distress of the cancer diagnosis, patients are most likely to become easily 'overwhelmed and ill-equipped to manage this complex multistep decision-making process' [27]. Other studies are in a similar vein [34, 47, 48]. Kim et al. conducted a survey completed by 204 participants. They found that 64% of them 'reported that they were too overwhelmed at the time of their cancer diagnosis to consider FP options' [47]. Logan et al. conducted a systematic literature review and found that some women with cancer endorsed the need for information at the time of diagnosis, with other women highlighting 'the importance of receiving fertility information during cancer treatment decision-making and in follow-up' [48].

Limitations

Most participants were recruited through the snowball sampling technique. This enhances the diversity of the study and can be regarded as a strength. Furthermore, the sample consisted of women with various types of cancer. This can be seen as a strength too. However, this study should be interpreted in light of certain limitations. Almost all participants were between 30 and 45 years old, with the exception of only

one participant who was a very young woman (eighteen years old). Moreover, potential self-selection bias cannot be ruled out. Women who were particularly interested in preserving their fertility are more likely to have responded to our call for research participation. In addition, recall bias cannot be excluded to some extent, at least with regard to certain findings. Finally, participants were not asked to give feedback, namely, to check the consistency between their intentions and the results obtained by the researchers. This fact limits the reliability of the study in terms of confirmability.

Conclusions

A variety of distinct themes and subthemes emerged from the analysis of the interview data. The cancer diagnosis emerged as a factor that considerably affects the women's attitudes towards biological parenthood: It can further increase their (strong) previous desire or decrease their previous (weak) desire. Women with a recent cancer diagnosis did not receive adequate and multidisciplinary counselling, including clear and adequate information. However, participants felt satisfied from the information they received because they received the information they wanted, either by asking questions or by being in denial to get informed (i.e. because they felt overwhelmed after the cancer diagnosis). Embryo cryopreservation emerged as a less desirable fertility preservation option for women with cancer. Participants showed respect for human embryos, not always for religious reasons. Surrogacy emerged as the last resort option for most participants. Religious, social or financial factors did play a secondary (if any) role in women's decision making about fertility preservation. Finally, male partners' opinions played a secondary role in most participants' decision making about fertility preservation. If embryo cryopreservation was the selected option, partners would have a say because they were involved with their genetic material. The findings that emerged from data analysis were partly consistent with prior literature. However, we identified some interesting nuances that are of clinical importance. The results of this study may serve as a starting point for future research.

Abbreviations

COS	Controlled Ovarian Stimulation
IVM	<i>In vitro</i> oocyte maturation
EFS	Event-free survival
FP	Fertility Preservation
ART	Assisted reproductive technologies
ASCO	American Society of Clinical Oncology
ESHRE	European Society of Human Reproduction and Embryology
ASRM	American Society for Reproductive Medicine
HCP	Health Care Professionals
Q-o-L	Quality of Life

Declarations

Availability of data and materials

The transcripts of the full interviews that were collected and qualitatively analysed in the current study are not available for reasons of confidentiality. The redacted transcripts that were used and analysed as part of the current study can be made available by the corresponding author upon reasonable request.

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Contributions

The authors A-MT and PV were jointly responsible for conceptualizing the study, conducting the data analysis and ethical analysis of the findings, writing the paper and reporting the study. A-MT interacted with the participants and performed the interviews and the transcriptions. ET performed the patient selection and consent to participate in the research. ET and VT assisted in the data analysis and revisions of the paper. All authors contributed to revising this paper and read and approved the submitted version. The authors A-M T and PV have contributed equally to this paper and are co-first authors.

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Ethics approval and consent to participate

Prior to participating in this study, the participants were given adequate information regarding the aim, procedure, nature and confidentiality of the study as well as the processing of the data in accordance with the ethical approval received for research involving human participants. Subsequently, the participants were asked to provide their informed consent. The authors confirm that informed written consent was obtained from all subjects and/or their legal guardian(s). Only subjects who voluntarily provided informed consent were included in the study. The study and consent procedure were approved

by the Ethical and Deontology Committee of the Medical School of the Aristotle University of Thessaloniki (Reference number: 3.663/2.5.2018) and the Scientific Committee of the “Papageorgiou” Hospital of Thessaloniki (Reference number: 297/14-05-2018). In addition, we confirm that all methods were performed in accordance with the relevant guidelines and regulations. The authors assert that all procedures conducted as part of this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the guidelines stipulated by the Helsinki Declaration of 1975 (as revised in 2008).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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