



Preservation of Childbearing Potential in Cancer Survivors: a Survey of Gynecologists' and Embryologists' Current Knowledge, Attitude, and Practice

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Abstract

Cancer is one of the life-threatening diseases, and cancer therapy may produce severe side effects such as impaired fertility. Saving childbearing potential after cancer treatment is of high importance to cancer survivors. This study assessed gynecologists' and embryologists' current practice, knowledge, and attitude concerning fertility preservation (FP) in cancer survivors. This current survey was performed on a convenience sample of 277 gynecologists and embryologists who attended large international congresses held across Iran. A 23-item self-administered questionnaire that included questions on knowledge, attitudes, and practice was used. Questions had either yes/no responses, or were answered based on a 4-point (1 to 4) Likert scored scale. Total mean score for knowledge of all FP options was 2.97 ± 0.62 . Total mean scores for knowledge of all FP options in gynecologists and embryologists were 3.03 ± 0.65 and 2.95 ± 0.61 , respectively ($p = 0.33$). These scores were above the median value of 2.5 obtained using the 4-point Likert scale. Participants regarded the patient age as the most important reason for discussing FP with patients (mean scores 3.74 ± 0.71 and 3.73 ± 0.52 for gynecologists and embryologists, respectively; $p = 0.93$). The majority of the participants (i.e., 95.2% (79 gynecologists) and 92.2% (166 embryologists)) referred cancer patients to centers providing FP services ($p = 0.15$). This sample of Iranian gynecologists and embryologists had considerable information on FP methods to develop appropriate attitudes and practices in relation to FP for cancer patients in order to prevent loss of fertility.

Keywords Fertility preservation · Oncofertility · Infertility · Cancer patient · Gynecologists

Introduction

One of the life-threatening diseases is cancer [1]. Due to early detection of cancer cases and progresses made in cancer treatment, cancer patients' survival rate and lifespan are increased [2–4]. However, reproductive lives of cancer survivors can be affected by efficient cancer therapies [5, 6]. Impaired fertility as one of the severe side effects of cancer therapy can target influence cancer survivors of reproductive age [7, 8]. Many cancer patients would prefer a biological child to adoption or third-party reproduction [9].

Saving childbearing potential after cancer treatment can be of high importance for many cancer survivors who are

uncertain about their fertility status or are diagnosed with infertility [2, 10, 11]. Fertility preservation (FP) techniques with the aim of storing the possibility of becoming parents in cancer patients or other patients with benign diseases improve patients' quality of life after cancer therapy [12]. The FP options that are currently available for pre- or post-pubertal women and men include ovarian transposition, cryopreservation of embryos after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI), vitrification of oocytes and sperm, and cryopreservation of ovarian and testicular tissue [6].

The American Society of Clinical Oncology (ASCO) and the American Society for Reproductive Medicine (ASRM) have recommended that, prior to cancer treatment, all side effects and complications of cancer treatments on fertility should be discussed with cancer patients of reproductive age. Also, all cancer patients should be referred to reproductive specialists at the earliest possible opportunity [5, 7, 13]. The existing literature shows that physicians tend to minimize any possible delay in cancer treatment of some patients [14]. To prevent negative experiences and future regret about FP

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decisions, it is important to explore health care providers' comprehension and awareness of FP issue and evaluate whether physicians discuss treatment-related infertility with the patients or recommend FP [15]. However, little is known about health care providers' knowledge about FP or their attitudes toward discussing this matter with patients, especially in less developed countries. This study, therefore, aimed at surveying gynecologists' and embryologists' current practice, knowledge, and attitude with respect to FP in cancer survivors.

Methods

Participants

In this questionnaire-based study, a convenience sample of Iranian gynecologists and embryologists who attended two large international congresses, which took place in Iran between May and September 2016, was recruited.

Study Questionnaire

Based on previous researches done in the USA [8, 16] and UK [17], as well as eight in-depth interviews conducted with a panel of embryologists, gynecologists, and oncologists familiar with FP techniques for patients with cancer, a 23-item self-administered questionnaire was developed to measure self-perception of knowledge and attitude of gynecologists and embryologists toward FP options for cancer patients. Feasibility, ease of understanding, and acceptability of the self-completed questionnaire were also tailored by a number of gynecologists, embryologists, and oncologists. In addition, clarity of the questions was reviewed and confirmed by non-physician staff. The components of the questionnaire were as follows. The first part of the questionnaire asked participants to provide demographic information (e.g., sex, age, marital status, and number of children). In the second section, participants were asked to indicate their knowledge of FP options (such as cryopreservation of ovarian tissue, oocyte, sperm and testicular tissue, IVF with embryo cryopreservation, pre-treatment with gonadotropin-releasing hormone (GnRH), and ovarian transposition) based on a 4-point Likert scales (1, 2, 3, and 4 for none, little, intermediate, and a lot, respectively) for knowledge assessment. The participants also responded to three yes/no questions concerning the availability of clinics providing FP services in Iran and updated information on national and global guidelines for FP. After that, the respondents answered the question "Do you need more information on FP options?" In the third part, eight questions investigated participants' attitude toward FP in cancer patients. The questions were as follows. "How important is to provide cancer patients with information on FP?" and "To how many

of your patients do you recommend the use of FP services to your patients?" The next question was "How does age (e.g., giving priority to cancer patients of childbearing ages), sex (e.g., giving priority to women), socio-economic status (e.g., considering the patient's ability to afford the treatment?), type of cancer, heredity (the possibility of transferring genes and traits attributed to cancer to the next generation), type of treatment, prognosis, being invasive, already-having children and time limits (for initiating treatment), affect your recommendation to a cancer patient with respected to the use of FP option? The participants indicated agreement with these questions as assessed by a four-point Likert scale (score 1-4 represented greatly, usually, rarely, and never, respectively)." Another question was "What is the best way to inform you about FP options?" Responders selected one or more choices among "congresses," "brochures," "scientific journals," "media," and "websites". There were two yes/no questions as follows. "Is this a matter of medical malpractice if a cancer patient experiences infertility due to not receiving information about the use of FP techniques?" and "Is it needed to have a fertility counselor present in cancer treatment centers?" The last questions enquired what has the priority between cancer treatment and starting FP after cancer diagnosis in case of any conflict between starting treatment and performing FP (responses: therapeutic measures, FP, and patient decision) and feasibility of FP techniques for cancer patients (responses: only on the basis of the research, both research, and practical, only practical). Participants were allowed to choose one choice. The fourth part examined the current practice behaviors of gynecologists and embryologists using the following two yes/no statements "I provide written educational content for cancer patients about FP" and "I give cancer patients enough information on well-equipped fertility centers that provide FP services and refer them to these centers."

Statistical Analysis

Frequencies were summarized for categorical variables. Continuous variables were expressed as mean \pm standard deviation (SD) and 95% confidence intervals (CIs). Chi-squared test of independence was done to assess relationships between categorical variables derived from answers to yes/no questions. Knowledge and attitude questions with 4-point Likert scale responses were compared using the independent samples *t* test. The means of these scores showed the knowledge and attitude of the studied population. Heeren and D'Agostino, in 1987, demonstrated that this *t* test is robust for ordinal-scaled data [18]. All analyses were carried out using STATA (version 12.0; Stata Corp LP, College Station, TX). *p* values of less than 0.05 indicated statistical significance.

Table 1 Demographic characteristics of the 277 gynecologists and embryologists participated in the current survey

		Gynecologists (n = 85) N (%)	Embryologists (n = 186) N (%)	p value ^a
Sex	Male	3 (3.5)	49 (26.3)	< 0.0001*
	Female	82 (96.5)	137 (73.7)	
Marital status	Single	21 (24.7)	95 (51.1)	< 0.0001*
	Married	64 (75.3)	91 (48.9)	
Has child/children	Yes	63 (74.1)	53 (28.5)	< 0.0001*
	No	22 (25.9)	133 (71.5)	

^ap value is obtained by chi-square. *p < 0.05 was statistically significant

Results

A total of 317 gynecologists and embryologists were given a questionnaire; among them, 277 (87.38%) responded and participated in this study. The mean age of participants was 37.07 ± 11.40 years (mean age of gynecologists and embryologists was 47.74 ± 11.9 and 32.47 ± 7.11, respectively); also, 54 (19.5%) participants were men and 223 (80.5%) were women. Of the participants, 85 (31.4%) were gynecologists and 186 (68.6%) were embryologists. Detailed characteristics of the participants are provided in Table 1.

Knowledge of FP

For questions concerning specialists' knowledge of FP options for cancer patients, questions with choices of 4-point Likert scale (1 = no knowledge, 2 = little knowledge, 3 = an intermediate level of knowledge, and 4 = a lot knowledge) were used. The median score was 2.5. A total mean score for knowledge of all FP options was 2.97 ± 0.62, which was above the median. Total mean scores for knowledge of all FP options in gynecologists and embryologists were 3.03 ± 0.65 and 2.95 ± 0.61, respectively (p = 0.33). Mean scores for knowledge of using GnRH among gynecologists and embryologists were 3.06 (95%CI, 2.12–4.0) and 2.57 (95%CI, 1.6–3.54), respectively, which was significantly different between these two groups of participants (p < 0.0001) (Table 2). As

seen in Fig. 1, 77 gynecologists (92.8%) and 166 embryologists (91.7%) declared that they need to obtain more information on FP techniques. There was no statistically significant difference in this respect between gynecologists and embryologists (p = 0.76). In response to the question of updated information on national guidelines for FP in cancer patients, 53 gynecologists (63.9%) and of 115 embryologists (65.7%) mistakenly stated that there were guidelines for FP in cancer patients in Iran (p = 0.78) (Fig. 2).

Attitude Toward FP

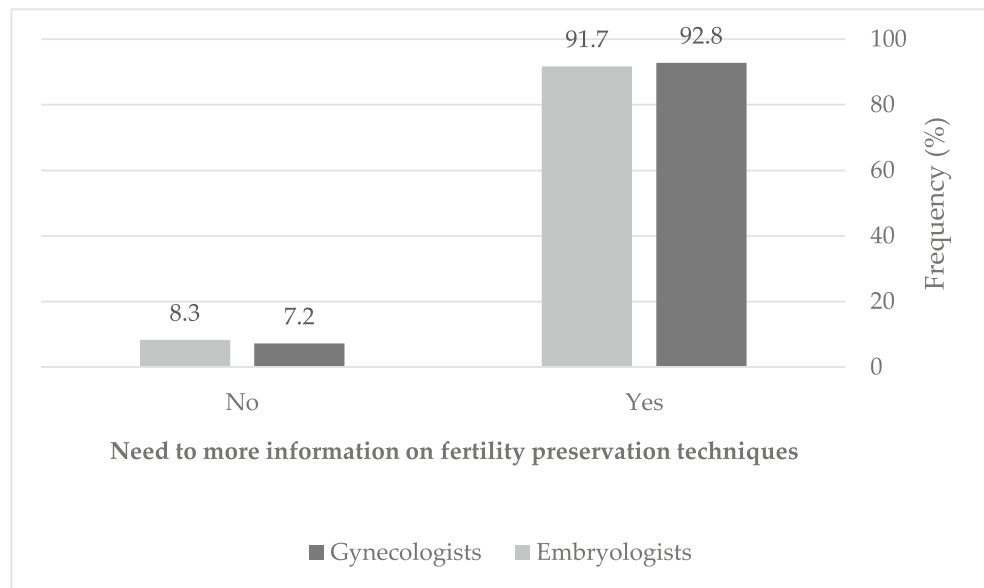
For questions on attitudes toward the use of FP techniques in cancer patients, 4-point Likert scale responses were 1 = never; 2 = rarely, 3 = usually to 4 = greatly were used. The median score was 2.5. A total mean score for questions on attitude concerning influential characteristics and clinical conditions of cancer patients in the use of FP techniques was 3.41 ± 0.56, which was above the median. Total mean scores for attitude of this question in gynecologists and embryologists were 3.41 ± 0.86 and 3.40 ± 0.43, respectively. No significant difference in attitude was found between gynecologists and embryologists (p = 0.94). According to Table 3, most of participants considered “age” the most important reason for discussing FP with patients (mean scores: 3.74 ± 0.71 and 3.73 ± 0.52 in gynecologists and embryologists, respectively (p = 0.93)). However, compared to gynecologists, a higher

Table 2 Comparison of participants' knowledge about fertility preservation option in cancer patients

Preserving fertility options	Gynecologists mean ± SD	Embryologists mean ± SD	p value ^a
Ovarian tissue cryopreservation	2.94 ± 0.85	2.94 ± 0.83	0.98
Oocyte cryopreservation	3.20 ± 0.85	3.18 ± 0.79	0.85
IVF with embryo cryopreservation	3.35 ± 0.90	3.15 ± 0.88	0.09
Ovarian transposition	2.57 ± 1.03	2.62 ± 0.91	0.71
Gonadotropin-releasing hormones (GnRH)	3.06 ± 0.94	2.57 ± 0.97	< 0.0001*
Sperm cryopreservation	3.11 ± 1.01	3.24 ± 0.89	0.27
Testicular tissue cryopreservation	2.73 ± 1.03	2.97 ± 0.90	0.06
Total mean score	3.03 ± 0.65	2.95 ± 0.61	0.33

^ap value is obtained by independent sample t test. *p < 0.05 was statistically significant

Fig. 1 Comparison of participants' awareness of their need to acquire more information on fertility preservation techniques ($p = 0.76$)



percentage of embryologists had the attitude that if there is a potentially heritable cancer, health care providers less likely offer FP options [3.56 (CI95%: 2.93–4.19) vs. 3.39 (CI95%: 2.61–4.17) for embryologists and gynecologists, respectively]; similarly, no significant difference was observed ($p = 0.078$).

Most participants regarded FP as an important issue [scores of 3.82 (CI95%: 3.44–4.2) for gynecologists and 3.79 (CI95%: 3.27–4.31) for embryologists ($p = 0.57$)] and would recommend such techniques to cancer patients [scores 3.68 (CI95%: 3.16–4.2) in gynecologists and 3.73 (CI95%: 3.18–4.28) in embryologists ($p = 0.49$)]. As seen in Table 4, most of respondents (i.e., 53 gynecologists (67.1%) and 144

embryologists (81.8%)) believed that post-cancer treatment infertility in cancer patients due to not providing them with information about the use of FP techniques is a medical malpractice; however, in this regard, a significant difference was found between gynecologists and embryologists ($p = 0.02$). The vast majority of the responding participants (i.e., 82 gynecologists (97.6%) and 183 embryologists (98.9%)) indicated that there is a need for the presence of a fertility counselor in cancer treatment centers. The two groups were not significantly different in this respect ($p = 0.41$). However, only 11 gynecologists and 27 embryologists (13.1 and 14.6%, respectively ($p = 0.74$)) preferred starting FP to cancer treatment after cancer diagnosis.

Fig. 2 Comparison of participants' perception that Iranian internal fertility preservation guidelines exist ($p = 0.78$)

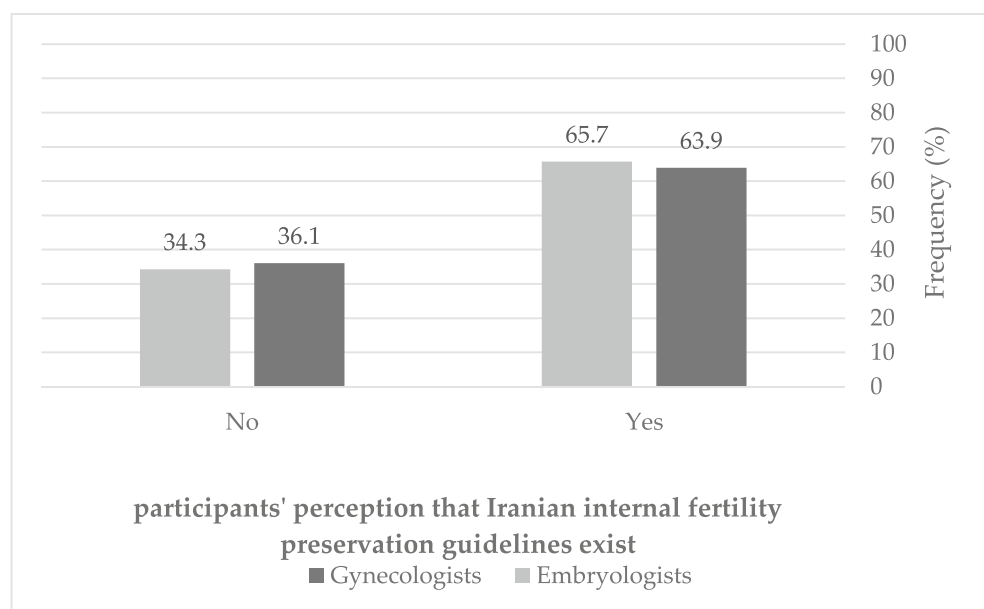


Table 3 Comparison of participants’ attitude toward characteristics and clinical conditions influencing the use of FP techniques in cancer patients

Influencing factors	Gynecologists mean ± SD	Embryologists mean ± SD	<i>p</i> value ^a
Age	3.74 ± 0.71	3.73 ± 0.52	0.93
Sex	3.18 ± 0.90	3.22 ± 0.89	0.75
Type of cancer	3.53 ± 0.81	3.60 ± 0.67	0.44
Heredity	3.39 ± 0.78	3.56 ± 0.63	0.07
Type of treatment	3.55 ± 0.71	3.66 ± 0.59	0.23
Poor prognosis	3.33 ± 0.87	3.23 ± 0.81	0.41
Being invasive	3.41 ± 0.96	3.56 ± 0.70	0.17
Marital status	3.24 ± 0.98	3.22 ± 0.88	0.90
Having a child or children	3.51 ± 0.59	3.01 ± 0.86	0.20
Socio-economic status	3.28 ± 0.91	3.32 ± 1.57	0.84
Time limitation for consultation with patient	3.16 ± 0.94	3.27 ± 0.81	0.35
Total mean score	3.41 ± 0.86	3.40 ± 0.43	0.94

^a *p* value is obtained by independent sample *t* test

Current Practice

As shown in Table 5, with regard to information provision for the patients, 44 gynecologists and 117 embryologists (52.4 and 67.6%, respectively (*p* = 0.06)) stated that they provided their patients with written information about FP. The majority (i.e., 95.2 (79 gynecologists) and 92.2% (166 embryologists) of respondents) gave information on fertility centers providing FP services to patients and referred them to these centers. No statistically significant differences were observed between gynecologists and embryologists in this respect (*p* = 0.15).

Discussion

To our knowledge, this study is the first published survey of Iranian gynecologists’ and embryologists’ knowledge and attitudes regarding post-cancer treatment infertility, and practices

regarding the use of FP approaches in cancer patients. The most important finding of the present study was that the majority of participants showed satisfactory information on all FP approaches, which was above the median value of 2.5. It was predictable that compared to embryologists, gynecologists had more information about GnRH. However, most participants were not aware of the lack of national FP guidelines in Iran. It is possible that respondents mistakenly considered ASCO and ASRM guidelines as national guidelines. The existing evidence and literature suggest that no study has assessed knowledge, attitude, and referral behavior of gynecologists and embryologists, as health care providers who play important roles in preserving fertility potential of cancer patients. The majority of the research assessed knowledge, perspectives, and referral practice of medical oncologists, radiation oncologists, hematologists, and pediatric oncologists [8, 17].

The findings of the current survey revealed that all responding participants believed that discussing FP with cancer patients and recommending it to them are

Table 4 Comparison of participants’ attitude toward importance of preserving fertility in cancer patients

	Gynecologists		Embryologists		<i>p</i> value ^a	
	Yes <i>N</i> (%)	No <i>N</i> (%)	Yes <i>N</i> (%)	No <i>N</i> (%)		
Medical malpractice for post-cancer treatment infertility due to not giving cancer patients information about the use of preserving fertility services	53 (67.1)	26 (32.9)	144 (81.8)	32 (18.2)	0.02*	
Need to a fertility counselor in cancer treatment centers	82 (97.6)	2 (2.4)	183 (98.9)	2 (1.1)	0.41	
Priority between cancer treatment and starting fertility preservation after cancer diagnosis	Therapeutic measures	49 (58.3)	35 (41.7)	115 (62.2)	70 (37.8)	0.55
	Fertility preservation	11 (13.1)	73 (86.9)	27 (14.6)	158 (85.4)	0.74
	Patient decision	27 (32.1)	57 (67.9)	49 (26.5)	136 (73.5)	0.34

^a *p* value is obtained by chi-square. **p* < 0.05 was statistically significant

Table 5 Comparison of participants' current practice about preserving fertility in cancer patients

	Gynecologists		Embryologists		<i>p</i> value ^a
	Yes <i>N</i> (%)	No <i>N</i> (%)	Yes <i>N</i> (%)	No <i>N</i> (%)	
Providing written educational content to the cancer patients about FP	44 (52.4)	40 (47.6)	117 (67.6)	56 (32.4)	0.06
Given information on fertility centers equipped to provide FP services and refer cancer patients to these centers	79 (95.2)	4 (4.8)	166 (92.2)	14 (7.8)	0.15

^a*p* value is obtained by chi-square

important issues. Also, they believed that chief barriers to discussion of the use of FP with cancer patients and not referring them to fertility clinics are risk of treatment delay, disease prognosis, and patient characteristics (e.g., gender, aggressiveness of cancer, low likelihood of survival, marital status, heredity, and number of children). These are perceived barriers that have been previously mentioned by other health care providers for initiating a discussion about FP [17, 19–21]. Being attentive to the availability of centers providing FP services and details like ethical, social, religious, and cultural issues is essential when discussing FP [22, 23].

The ASCO and ASRM guidelines have emphasized that health care providers have a responsibility to inform patients that receive cancer treatments that may affect fertility [7]. In the present survey, the majority of participants considered cancer treatment-related infertility due to not giving cancer patients information about the use of FP techniques, “medical malpractice.” It is worth noting that in case of any conflict between starting treatment and performing FP (FP would postpone the treatment which needs to be started fast), the majority of participants insisted on starting the cancer treatment after cancer diagnosis rather than suggesting FP. Some participant made no difference in their recommendations to the patients between these two choices and left the decision totally to the patients.

Many reproductive age patients are not referred to see a reproductive specialist and referrals are inconsistently made. Cancer treatment may be started without opportunity for preserving fertility [24]. Findings of the current survey suggest that the vast majority of respondents declared that they give information on equipped fertility centers that provide FP services and referred cancer patients to these centers. Extensive knowledge of fertility is not essential for discussing cancer treatment-related infertility with patients, but it is important that a physician knows where the patients should be referred to [17].

Limitation

The current survey had several limitations. First is the possibility of selection bias in our study population: The

results of this study might be influenced by the fact that all participants were recruited from international congresses and may therefore be well-informed about the recent advances in this field than other physicians. So, the findings might not be fully representative of the entire population of gynecologists and embryologists in Iran. According to a high response rate (87%), any impact is likely to be relatively minor. Second is the reporting bias: the self-reported nature of the survey may have led to an over estimation of FP behavior of participants and so may not be representative of actual practice. However, since few objective measures of FP knowledge and attitudes among participants are available from routine data, this is an unavoidable limitation.

Conclusion

This study documented knowledge, attitudes, and practices concerning fertility preservation in cancer patients, among a sample of Iranian gynecologists and embryologists. Results of the current study showed that responding participants had satisfactory information on all FP options; however, the participants declared that they are in need for more information on FP. Insight into priority of starting FP to cancer therapy can be improved by disseminating treatment-related infertility and FP information, through brochures, published resources, or further education. This in turn should help gynecologists and embryologist to develop appropriate attitudes and practices toward FP for cancer patients and prevent loss of fertility.

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Compliance with Ethical Standards

Ethical approval was obtained from the Ethics Committee of the Royan Institute (IR.ACER.ROYAN.REC.1395.99). The aims of the study were clearly explained to all participants prior to the investigation, and confidentiality and anonymity were assured. Also, all participant voluntarily completed the questionnaire.

Conflict of Interest The authors declare that they have no conflict of interest.

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