



MONITOR 25: A Pilot Survey among Health Care Professionals Regarding Fertility Preservation Counseling in Gynecological Cancer Patients

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Abstract

The aim of this survey was to evaluate the existing knowledge, attitudes, and practices of physicians regarding fertility preservation measures.

Design: An anonymous online survey comprising 50 items was disseminated from 09/2021 to 12/2023.

Results: 54 physicians specializing in gynecology and obstetrics in Germany completed the questionnaire. 40% of respondents indicated that they provided minimal counseling to their patients due to a lack of knowledge, priority, and/or time constraints. The referral rate to a reproductive medicine specialist was <20%. Most respondents found the existing courses and training to be insufficient. 80% expressed interest in additional courses or training. Participants deemed fertility preservation feasible in the following scenarios: 88% for borderline ovarian tumors, 67% for endometrial cancer G1 or malignant ovarian cancer TNM stage pt1a, 20% for TNM stage pT1b, and only 18% for TNM stage pt1c. Regarding fertility preservation in cervical cancer (L0, V0, N0), 63% considered it feasible for tumor sizes < 4cm, while only 12% did so for sizes > 4cm. Anti-Müllerian hormone measurements were the most commonly used method for assessing ovarian reserve.

Conclusion: The rate of counseling on fertility preservation and referrals to specialists remains notably low due to inadequate knowledge, prioritization, and/or time constraints. Furthermore, the current survey underscores the pressing need for enhanced training and education in oncofertility among healthcare professionals, given participants' evident interest in expanding their understanding of fertility-sparing surgery and preservation techniques.

Introduction

Oncological advancements have led to improved outcomes for cancer patients, resulting in higher survival rates. Consequently, the importance of fertility preservation measures,

which offer the possibility of childbearing after cancer therapy, has become increasingly significant [1]. Depending on the type and severity of cancer, patients may be presented with various options for fertility preservation, including less invasive surgical procedures, oocyte or embryo preservation, ovarian tissue



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preservation, ovarian transposition prior to radiation, or the use of medications such as GnRH analogs to safeguard ovarian function, or a combination of these approaches [2-6]. However, methods like oocyte or embryo cryopreservation typically involve a minimum two-week period of ovarian stimulation with gonadotropins, followed by follicle aspiration, potentially delaying initiation of anti-cancer treatment. In cases where the cancer is particularly aggressive, physicians may choose to immediately proceed with anti-cancer treatment after preserving ovarian tissue via laparoscopy [2-6].

Despite 40-60% of cancer patients of reproductive age being counseled about fertility preservation options, only 4% actually utilize these methods [1]. Therefore, this study aims to investigate the current knowledge, attitudes, and practices of physicians regarding fertility preservation measures in gynecological cancer patients. Additionally, it seeks to assess the need for further training, networking, and counseling concerning fertility-sparing and preservation techniques.

Material and Methods

Prior to commencing the study, approval was obtained from the Ethics Committee of Charité. A multi-center nationwide survey was conducted among physicians specializing in gynecology and obstetrics across Germany. The survey was administered online at various hospitals and conferences from September 2021 to December 2023. A multiple-choice questionnaire comprising 50 items was developed to elicit information on the current knowledge, attitudes, and practices of physicians regarding fertility preservation measures in gynecological cancer patients. The selection of questions was based on a review of the most pertinent publications in this field. This project was adapted from the NOGGO (Nord- Ostdeutsche Gesellschaft für Gynäkologische Onkologie = North-Eastern German Society for Gynaecological Oncology).

The questionnaire was divided into three main sections: The first section gathered information on respondents' demographics such as gender, current position, and professional experience. The second section focused on personal expertise and practices related to fertility preservation counseling. Questions addressing potential biases in fertility preservation counseling, such as patient age, marital status, sexual orientation, and socioeconomic status, were included. The third section queried respondents about their personal opinions regarding fertility preservation measures, as well as procedures not yet legalized or established in Germany.

A pilot phase involving interviews with 10 physicians was conducted to confirm the comprehensibility and feasibility of the questionnaire.

Categorical data were presented as absolute counts with corresponding percentages.

Results

Demographic Characteristics

A total of fifty-four doctors specializing in gynecology and obstetrics in Germany participated in the survey. Among them, 52% are currently employed in the city-state of Berlin.

Seventy percent of the doctors are working in hospitals. Within this group, the majority are employed at centers of maximum care or university hospitals. The remaining doctors work in outpatient clinics. Notably, 67% of the hospitals or medical

practices do not provide specialized care in reproductive medicine.

The majority of respondents are either specialists in gynecology and obstetrics (43%) or resident doctors (30%). The remaining respondents are chief physicians (9.25%) and consultants (18.5%). Regarding years of experience, 20% of respondents have 0-5 years, 33% have 5-10 years, and 44% have more than 10 years of experience practicing medicine.

The fields of sub-specialization among respondents include gynecological oncology (27%), reproductive medicine (17%), obstetrics/perinatal medicine (6%), and none (50%).

Eighty percent of respondents identified as female, 17% as male, none as non-binary, and 3.7% did not provide an answer. The majority of participating doctors (60%) have children, whereas only 12.5% have utilized the services of a reproductive medicine specialist. The vast majority of participants rated having children as personally and professionally important for themselves and their patients.

For a detailed breakdown of demographic characteristics, refer to Table 1.

Table 1: Characteristics of respondents.

characteristics	subcategory	n	percentage
respondents		54	100%
gender	female	43	80%
	male	9	17%
	non-binary	0	0%
	no answer	2	3.7%
current position	chief physician	5	9.25%
	consultant	10	18.50%
	specialist in gynecology and obstetrics	23	42.60%
	resident doctor	16	29.60%
	no answer	0	0%
currently working at	hospital	38	70.4%
	outpatient-clinic	16	29.6%
	no answer	0	0%
hospital of	primary/ standard care	2	3.7%
	specialized care	5	9.3%
	maximum care or university hospital	31	75.6%
	no answer	16	29.6%
professional experience	0 - 5 years	11	20.40%
	5 - 10 years	18	33.30%
	> 10 years	24	44.40%
	no answer	1	1.85%
sub-specialization	reproductive medicine and endocrinology	9	16.70%
	gynecological oncology	14	25.93%
	perinatal medicine	3	5.5%
	no sub-specialization	26	48.15%
	no answer	2	3.7%

Expertise in the Field of Fertility Preservation

When asked to rate their expertise in two areas-(a) fertility-sparing surgery in gynecological oncology and (b) fertility-sparing measures such as cryopreservation of ovarian tissue or

oocytes, and medication for gynecological cancer patients-on a scale from 1 (very low/none) to 10 (very high/expert), respondents reported median scores of 4.4 for the former and 5.2 for the latter.

Counseling on fertility preservation

A majority of respondents (63%) provided counseling on fertility preservation to gynecological cancer patients. Regarding the percentage of patients counseled, 40% of respondents reported counseling a relatively low number (10-19%) of their patients, while 34% reported counseling almost all (80-100%) of their gynecological cancer patients (see Figure 1). Among the nine respondents with a subspecialty in reproductive medicine, 79-100% counseled their patients on fertility preservation options. Additionally, 85% of participants collaborated with referral centers that offer fertility-preserving measures. However, the referral rate of gynecological cancer patients to a reproductive medicine specialist was below 20%.

Barriers to counseling

When asked about reasons for not providing counseling on fertility preservation to gynecological cancer patients, responses were evenly distributed among lack of knowledge, lack of priority, and lack of sufficient time (see Figure 1). Notably, lack of financial compensation for counseling was not identified as a primary reason.

FertiPROTEKT network awareness and participation

An overwhelming majority of respondents were familiar with the FertiPROTEKT network, and half of the participating clinics and hospitals were members. Established in 2006, the FertiPROTEKT network encompasses all German-speaking countries (Germany, Austria, Switzerland) and provides fertility-sparing measures to women and men undergoing gonadotoxic treatments. The network also offers information, guidance, and supports scientific research.

Need for training and networking

Eighty-one percent of participants expressed a desire for more knowledge regarding reproductive measures (see Figure 2). The current availability of courses and training on “fertility and cancer” was deemed insufficient by 65% of respondents (see Figure 2). Additionally, 80% of participants showed interest in more courses or training, preferring formats such as webinars, followed by in-person training courses and rotations to specialized centers (see Figure 2).

Reproductive measures in Gyneco-oncological patients

Participants considered fertility preservation feasible in the following conditions: 88% in cases of borderline ovarian tumors, 67% in endometrial cancer G1 or malignant ovarian cancer at TNM stage pT1a, 20% at TNM stage pT1b, and only 18% at pT1c. For cervical cancer (L0, V0, N0), 63% of respondents regarded fertility preservation as feasible if the tumor size was below 4 cm, but only 12% considered it feasible if the tumor size exceeded 4 cm.

Serum Anti-Müllerian Hormone (AMH) measurements were the most frequently used method to assess ovarian reserve. Additionally, 50% of respondents used antral follicle counts or measurements of FSH, LH, and estrogen for this purpose. When deciding to offer cryopreservation of ovarian tissue, 31% of respondents followed the Edinburgh criteria, hospital or department guidelines, or personal assessment, respectively.

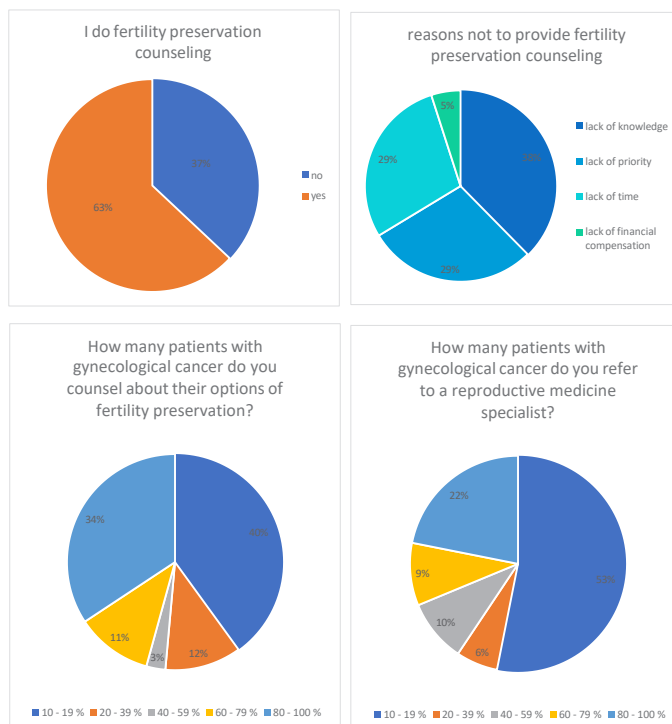


Figure 1: Details of fertility preservation counseling.

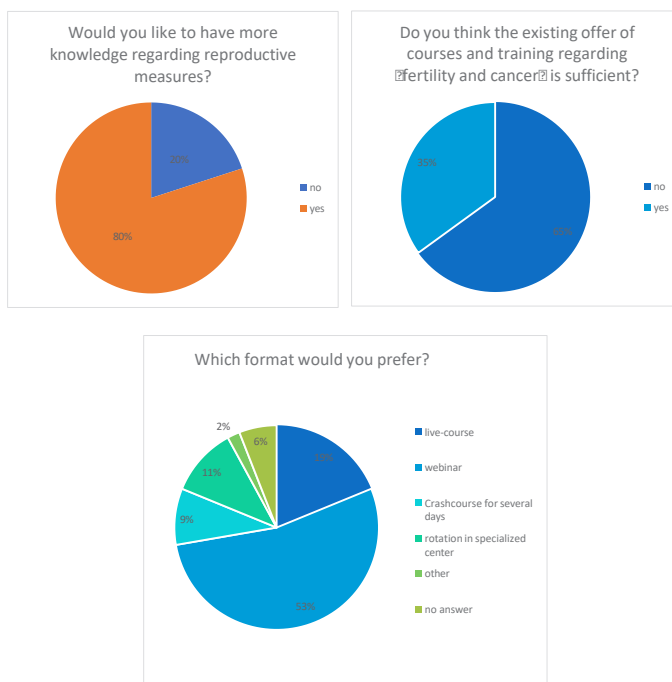


Figure 2: Interest in expanding knowledge regarding knowledge on “fertility and cancer”.

The most frequently recommended fertility preservation measure was cryopreservation of oocytes after hormonal stimulation (73.5%), followed by cryopreservation of ovarian tissue (65%), use of GnRH (Gonadotropin-Releasing Hormone) analogues for ovarian protection during chemotherapy (59%), and ovarian transposition surgery prior to pelvic radiation (55%). Cryopreservation of oocytes was also considered the most effective method for achieving a future pregnancy by 81% of respondents.

Regarding age limits for offering fertility preservation, 56.5% of respondents considered 40 years as the upper limit, while a quarter would offer it to women up to 45 years (2% set the limit at under 30 years, 17% under 35 years).

Most respondents (87%) fully agreed that fertility-preserving measures should be offered to patients with a very good disease prognosis. Furthermore, 67% agreed to offer these measures to patients with a risk of amenorrhea greater than 20%, and another 67% to patients who do not have children. Sixty-five percent supported fertility-preserving measures if the effectiveness of cancer therapy remained unaffected, while only 43% supported them if they did not cause any additional delay in oncological therapy. Most doctors indicated that factors such as low socioeconomic status, different cultural backgrounds, language barriers, homosexuality, or current single status would not significantly influence their decision to provide counseling on fertility preservation.

Sixty percent of participants viewed the prospect of a future pregnancy in a patient with a history of a hormone-receptor positive tumor as somewhat to very secure, while approximately 23% disagreed, and about 18% remained neutral. Regarding the safety of assisted reproductive technologies such as IVF, ICSI, or hormonal stimulation in patients with a history of hormone-receptor positive tumors, 68% considered it rather to very secure. Approximately 18% disagreed, and 15% remained neutral.

Discussion

The objective of this survey was to provide a comprehensive overview of current practices regarding fertility preservation counseling for gynecological cancer patients in Germany.

Despite the existence of European and German guidelines, our study highlights that many patients still do not receive adequate counseling or referrals to reproductive medicine specialists.

The ESMO guideline emphasizes that “all cancer patients of reproductive age should receive complete oncofertility counseling as early as possible in the treatment planning process, irrespective of the type and stage of the disease” [3]. Additionally, it suggests that “all patients with a potential interest in fertility preservation should be referred immediately to an appropriate fertility specialist/unit” [3].

The German FertiPROTEKT network recommends fertility-preserving measures under certain conditions: (a) when there is a good chance of survival, (b) when the risk of permanent amenorrhea is above 20%, and (c) when these measures are feasible and pose no major risk to the patient. Gonadotoxicity is typically assessed based on the risk of developing chemotherapy-induced amenorrhea (CIA). While temporary CIA is common after chemotherapy, the risk of persistent amenorrhea over 6-12 months is categorized as high (>80%), medium (40-60%), or low (<20%). Permanent amenorrhea not only affects fertility desires but also increases the risk of osteoporosis, cardiovascular disease, and has significant psychosocial implications [4,5].

In Germany, subspecialties such as gynecology, perinatal medicine, and reproductive medicine are often distinct. Given that most gynecological cancer patients are treated in certified cancer centers, their access to fertility preservation depends heavily on referrals to reproductive medicine specialists. However, the rate of referral for gynecological cancer patients to such specialists was found to be below 20%, aligning with reported rates in existing literature [7]. While 34% of respondents in our study provided fertility preservation counseling to nearly all of their patients, 40% counseled nearly none. Reported rates of counseling on fertility preservation vary, ranging from ap-

proximately 40% in the United States to 70% in Dutch cancer patients [7,8].

When asked about reasons for not providing counseling on fertility preservation to gynecological cancer patients, responses were evenly distributed among lack of knowledge, lack of prioritization, and lack of time. Our findings reveal a persistent knowledge gap concerning the tumor types and stages where fertility preservation could be offered. There was an overestimation of the prognosis and severity of disease in borderline tumors, ovarian, cervical, or endometrial cancer with the aforementioned tumor stages. According to German guidelines, except for cervical cancer with a tumor size exceeding 4 cm, fertility-sparing measures are feasible in all the mentioned tumor stages [4]. Moreover, a significant number of respondents did not utilize objective criteria in the decision-making process regarding which patients should receive counseling. The upper age limit for offering fertility preservation varied significantly among respondents. While the majority (56.5%) considered 40 years as the cutoff, a quarter of respondents would extend it to women up to 45 years of age (2% considering <30 years, and 17% considering <35 years).

According to the ESMO guideline, oocyte or embryo cryopreservation is recommended for women below 40 years of age, while ovarian tissue cryopreservation is suggested for those below 36 years of age [3].

Among the fertility preservation measures, cryopreservation of oocytes after hormonal stimulation was the most commonly recommended (73.5%), followed by cryopreservation of ovarian tissue (65%). These recommendations align with German and European guidelines, which indicate live birth rates exceeding 60% when 12 oocytes are cryopreserved in women under 35 years of age and approximately 40% when 10 oocytes are cryopreserved in women over 35 years of age [3]. To date, more than 300 women worldwide have undergone cryopreservation of ovarian tissue, with ovarian function restoration achieved in 95% of cases within 4-9 months. However, the duration of ovarian function restoration after grafting varies significantly, lasting from a few months to several years [3]. This procedure has resulted in the birth of over 180 babies, with live birth rates per woman around 40%, half of which were from natural conceptions [3].

To maximize chances of a successful future pregnancy, double stimulation can be considered to increase the number of retrieved oocytes. However, this approach requires approximately 4 weeks and is typically reserved for specific circumstances due to its time constraints. Another strategy to optimize the likelihood of pregnancy involves a combination of methods: Laparoscopic removal of ovarian tissue followed by hormonal stimulation and retrieval of oocytes [3].

For the protection of ovaries from radiation, two primary options are available: Ovarian transposition, preferably performed via laparoscopy, and the use of gonadal shielding during radiation therapy [3].

Responses from our survey indicate uncertainty regarding the use of hormonal stimulation in hormone-receptor positive tumors. Nevertheless, existing literature suggests that these procedures are relatively safe. In estrogen-sensitive tumors, a reduction in estradiol concentration can be achieved through co-treatment with aromatase inhibitors (e.g., letrozole at a dose of 2 x 2.5 mg/day) or tamoxifen [3].

The majority of surveys published in the literature refer to fertility preservation in breast cancer patients [9]. In these patients, ovarian suppression with gonadotropin-releasing hormone analogs during chemotherapy was the most commonly suggested strategy. Around 40% of respondents in this survey expressed dissent or uncertainty regarding ovarian stimulation and pregnancy in breast cancer patients [9].

Our survey underscores the pressing need for enhanced training and education in the field of oncofertility. Study participants displayed a high level of interest in expanding their knowledge of fertility-sparing surgery and preservation techniques for young cancer patients (80%).

This emphasis on education is crucial, as the decision to offer counseling on fertility-sparing surgical techniques or preservation methods such as cryopreservation of ovarian tissue or oocytes/embryos significantly impacts not only tumor prognosis, but also the incidence of premature ovarian insufficiency, menopausal symptoms, osteoporosis, sarcopenia, and cardiovascular risk profiles. Moreover, it contributes to lower levels of psychological distress among patients [10,11]. Even if patients ultimately decide against fertility preservation after receiving counseling, their satisfaction with and adherence to oncological treatment tends to improve [10,11]. Active involvement in decision-making and feeling well-informed about their options also contribute to an enhanced quality of life for patients [10,11].

Limitations of the study

One limitation of our study is the relatively low number of respondents, which may affect the generalizability of our findings. Despite distributing the survey at multiple conferences and workshops, the limited response rate indicates a lack of attention to this topic within the professional field in Germany. However, our study may help address specific questions regarding fertility preservation counseling, given the scarcity of data in the literature and the inadequacy of previous surveys on the subject.

It's important to note that our results are specific to the situation in Germany. They highlight gaps in the academic education of gynecologists during their training. Additionally, the separation between subspecialties such as gynecological oncology and reproductive medicine might contribute to the low referral rates observed in our study. These contextual factors should be considered when interpreting our findings.

Capsule: The present survey underscores the imperative for enhanced training, as participants exhibit a significant interest in augmenting their understanding of fertility-sparing surgery and fertility preservation techniques.

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J Sehoul: project development, survey distribution, manuscript editing, oversight.

Attestation statements

Data has not been previously published.

Data will be made available to the editors of the journal for review or query upon request.

Data sharing statement: Data will be shared upon request.

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