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Practice guidelines

Practice guideline on ovarian tissue cryopreservation and transplantation in the prevention and treatment of iatrogenic premature ovarian insufficiency☆

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ABSTRACT

Premature ovarian insufficiency (POI) refers to the decline of ovarian function before the age of 40. POI causes a reduction in or loss of female fertility, accompanied by different degrees of menopausal symptoms, which increases the risk of chronic diseases related to early menopause and seriously affects patients' quality of life and health. It is conservatively estimated that at least one million prepubertal girls and women of reproductive age in China are at risk of iatrogenic POI caused by radiotherapy and chemotherapy every year. With the development of medical technology and the breakthrough of scientific and technological advances, preventing and treating iatrogenic POI have become possible. International and national guidelines consider cryopreserved ovarian tissue transplantation to be the most promising method of preserving the ovarian function and fertility of prepubertal girls and women of reproductive age who cannot delay radiotherapy and chemotherapy. In order to guide the clinical application of ovarian tissue cryopreservation and transplantation technology in China, the Guideline Working Group finally included 14 scientific questions and 18 recommendations through a questionnaire survey, field investigation, and consultation of a large number of Chinese and English literature databases in order to provide a reference for colleagues in clinical practice.

1. Introduction

Premature ovarian insufficiency (POI) refers to the decline in ovarian function before the age of 40. Traditionally, the prevalence rate of POI is about 1 %. Recently, it has been reported that the prevalence rate of POI has increased significantly, reaching 3.7 % ~ 10 % [1,2]. POI can cause the decrease or loss of female fertility, accompanied by different degrees of peri-menopausal symptoms. In addition, the fluctuation of estrogen levels can increase the risk of cardiovascular diseases, osteoporosis, Alzheimer's disease and other diseases, significantly shorten life expectancy and seriously affect patients' quality of life and health [3]. Iatrogenic POI refers to ovarian dysfunction related to medical care behaviour. The common causes are surgery, chemotherapy, radiotherapy and intake of other ovarian toxic substances, accounting for about 50 % of POI [4,5].

According to data from the World Health Organization (WHO), there are >4.5 million new cancers in China annually. It is conservatively estimated that at least one million prepubertal girls and women of reproductive age in China are at risk of iatrogenic POI due to radiotherapy and chemotherapy every year and should be evaluated to preserve ovarian function and fertility. Therefore, it is very important to prevent the occurrence of iatrogenic POI effectively [6]. It is internationally agreed that ovarian tissue cryopreservation and transplantation (OTCT) is the only method to preserve ovarian function and fertility in children and women of reproductive age who cannot delay radiotherapy and chemotherapy, and it is also the most effective and promising method to preserve ovarian function and fertility at present [7,8]. Multidisciplinary experts were asked to join a working group to formulate this guideline to better guide the clinical application of OTCT in the prevention and treatment of iatrogenic POI.

The guideline working group collected clinical issues of concern to clinicians and patients through questionnaires. The survey collected 500 doctors' and 300 patients' questionnaires from 34 provinces, autonomous regions and municipalities directly under the Central Government and combined them to remove duplicates. According to their importance ranking and the feasibility of literature retrieval, the guideline working group finally decided to include 14 clinical questions after further discussion. This guideline comprises 14 clinical questions and 18 recommendations. The evidence level (Table 1) and recommendation level (Table 2) refer to the standards of the Oxford Center for Evidence-based Medicine in 2009 [9] and are marked in brackets after each recommendation.

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Table 1
The level and meaning of evidence used in this guide.

Level of evidence	Meaning
1a	Homogeneous randomized controlled trials, initial cohort, prospective cohort, systematic review of level 1 diagnostic studies, multi-population based studies, multicenter studies
1b	Randomized controlled trial with a narrow confidence interval, follow-up >80 %, single population, single-center study
1c	Evidence that the observation result is "all or no."
2a	A systematic review of homogeneous cohort studies, retrospective cohorts of randomized controlled studies, and diagnostic studies above grade 2
2b	1 cohort (including low-quality randomized controlled studies), retrospective cohort, poor follow-up
2c	Outcome study
3a	Systematic review of homogeneous case-control studies
3b	1 case-control study, discontinuous study
4	Case series study, low-quality cohort study, or case-control study
5	Expert opinion, no clear, rigorous evaluation, basic research based on laboratory

Table 2
Recommended levels and meanings used in this guide.

Recommended grade	Meaning
A	Consistent Level 1 evidence
B	Consistent Level 2 or Level 3 evidence or inference of Level 1 evidence
C	Level 4 evidence, or level 2 or level 3 evidence inference
D	Level 5 evidence, or inconsistent or uncertain conclusions

2. Ovarian tissue cryopreservation

2.1. Which population is suitable for ovarian tissue cryopreservation?

Ovarian tissue cryopreservation (OTC) refers to removal of ovarian tissue followed by cryopreservation based on the principle of cryobiology. It is the only choice to preserve ovarian function and fertility in prepubertal girls and women of reproductive age who cannot delay radiotherapy and chemotherapy. It does not require ovarian stimulation and delay follow-up treatment, preserves thousands of follicles at one time, preserves fertility, and restores ovarian endocrine function to a certain extent [10,11]. OTCT has been formally used in clinical practice and is no longer an experimental technology, which is the main method to prevent and treat iatrogenic POI [7]. If the patient has received low toxicity and low-dose chemotherapy, the ovarian function of the patient should be evaluated to judge whether OTC can be performed, and chemotherapy before OTC should not be regarded as a contraindication [7,12,13].

Recommendation 1–1: Ovarian tissue cryopreservation is suitable for preserving ovarian function and fertility in patients with tumour and non-tumour diseases and is the only preservation method of ovarian function and fertility for prepubertal girls and women of reproductive age who cannot delay ovarian toxicity treatment. (2b, B).

Recommendation 1–2: Chemotherapy before OTC should not be considered a contraindication to ovarian tissue cryopreservation. (2b, B).

2.2. What are the cautions for ovarian tissue sampling surgery?

In principle, an ovarian tissue biopsy should be taken before radiotherapy and chemotherapy or at the same time as pelvic surgery. If the patient has received low toxicity and low-dose chemotherapy, the ovarian function of the patient should be evaluated to judge whether OTC can be performed. The sampling plan is made individually according to the risk of iatrogenic POI and ovarian reserve function. Generally, at least 1/2 or 2/3 of one ovary or 1/2 of both ovaries are biopsied. Because of the small size of the ovary in prepubertal girls, a unilateral oophorectomy is recommended.

It is suggested that qualified units should use a laparoscope to biopsy ovarian tissue or perform biopsy at the same time as laparotomy, the corpus luteum should be avoided as much as possible, a cold knife should be used, surgical energy devices should not come into contact with the ovary, thermal injury should be avoided and the integrity of the biopsied ovarian tissue should be ensured. Surgical energy devices can be used in children when removing a unilateral ovary, but heat injury must be eliminated and ischemic and mechanical injuries such as clamping and extrusion for a long time should be avoided.

To avoid warm ischemia injury, ovarian tissue should be put into hypothermic transfer fluid immediately. The hospitalization time of laparoscopic ovarian tissue sampling surgery ranges from 1 to 3 days. There is no report of intraoperative and postoperative ovarian tissue sampling surgery complications, which can be managed according to general laparoscopic examination [10,14–17].

Recommendation 1–3: Ischemia, mechanical injury and thermal injury must be avoided during ovarian tissue biopsy. (1c, A).

2.3. Which freezing method should be used for ovarian tissue cryopreservation?

OTC methods include slow freezing and vitrification. At present, the standard method of OTC worldwide is slow freezing [7,10,12,18]. From over 200 babies born after OTCT worldwide, only two live births are realized by vitrification of ovarian tissue [18,19].

Recommendation 1–4: Slow-freezing is the standard method of ovarian tissue cryopreservation, and vitrification of ovarian tissue is still a clinical study. (1a, A).

3. Ovarian tissue transplantation

3.1. Is there a risk of recurrence of primary disease in patients with malignant tumours undergoing ovarian tissue transplantation?

Gellert et al. reported monitoring ovarian tissue transplantation from 21 countries; no disease recurrence was caused by ovarian tissue transplantation [20]. According to the data from five European centers in 2021, there is no correlation between the recurrence risk of primary disease and OTCT [12]. For patients with a high risk of ovarian contamination such as leukemia, OTC after chemotherapy to complete remission can significantly reduce the risk of ovarian contamination [21–24].

Evaluating the safety of patients with malignant tumours before ovarian tissue transplantation is very important. Histological microscopy, immunohistochemical staining, fluorescence in situ hybridization (FISH), real-time fluorescence quantitative reverse transcription polymerase chain reaction, etc., can screen specific markers of primary tumours at the cellular or molecular level. For patients lacking specific tumour markers, multicolour flow cytometry can also be selected to detect ovarian tissue. Xenotransplantation experiments in immunodeficient mice are important methods for evaluating the recurrence risk of ovarian tissue implantation in tumour patients, which can evaluate the potential risk of tumour recurrence. The above assessment methods provide risk assessment for tumour patients with a high risk of ovarian contamination [25–27]. After ovarian tissue transplantation, besides the follow-up of ovarian function recovery, the primary disease should be followed up routinely.

In ovarian tissue preparation, immature oocytes in ovarian tissue are cultured in-vitro and cryopreserved. This can improve the fertility preservation efficiency of patients and is also a safe choice for patients with a high risk of ovarian contamination [28–31].

Recommendation 2–1: The risk of recurrence of primary disease after cryopreserved ovarian tissue transplantation is very low. (3b, B).

Recommendation 2–2: Safety assessment of tumour contamination should be carried out before cryopreserved ovarian tissue transplantation. (3b, B).

Recommendation 2–3: For patients with a high risk of cryopreserved ovarian tissue transplantation such as leukemia, cryopreservation of ovarian tissue after chemotherapy to complete remission can reduce the risk of cryopreserved ovarian tissue transplantation. (4, C).

3.2. How should the timing and indication of ovarian tissue transplantation be determined?

Transplantation time should be determined according to whether the patient's primary disease is cured, whether clinical rehabilitation is performed, whether full communication with the patient is possible, and what the individual situation is after multi-disciplinary consultation. Generally, the primary disease is relieved, and patients have peri-menopausal symptoms related to ovarian function decline, such as hot flushes and sweating, serum follicle-stimulating hormone (FSH) $\geq$ 25 IU/L or serum anti-Muellerian hormone (AMH) $<$ 1.1 ng/mL. After stop of ovarian toxicity treatment for at least 3–6 months, ovarian tissue transplantation can be considered [10,11].

Recommendation 2–4: Ovarian tissue transplantation should be considered at least 3–6 months after completion of radiotherapy and chemotherapy for tumour patients. (2b, B).

Recommendation 2–5: The timing of ovarian tissue transplantation should be decided after a multi-disciplinary consultation. (4, C).

3.3. Can transplantation of cryopreserved ovarian tissue restore ovarian function?

Gellert et al. reported that ovarian function recovered in 95 % of the 318 OTCT women worldwide [20]. 285 women from five European centers were followed up after OTCT, and the recovery rate of ovarian endocrine function in the center with the highest recovery rate was 97 % [12]. OTCT has been performed in 19 patients in China's first ovarian tissue cryobank, and the recovery rate of ovarian function after surgery is as high as 100 % [32].

A meta-analysis showed that the median time for ovarian function to return to normal was 19 weeks [19]. In China's first ovarian tissue cryobank, all patients who underwent OTCT recovered their ovarian function within 3–4 months [32].

Before and after cryopreserved ovarian tissue transplantation, ovarian function in patients with peri-menopausal and menopausal-related symptoms due to POI may not have returned to normal. If there is no contraindication, menopausal hormone therapy (MHT) can be considered. Traditional Chinese medicine is widely used in clinics as one of the drug therapies for POI. Those with MHT contraindications or fear of MHT can reasonably choose traditional Chinese medicine, such as Kuntai capsules. Alternative therapies, such as botanical drugs, can also be selected according to the patient's situation [32,33].

Recommendation 2–6: Cryopreserved ovarian tissue transplantation can restore ovarian function. (2b, B).

3.4. Can cryopreserved ovarian tissue transplantation be used to induce puberty development?

Impaired ovarian function and decreased fertility are among the most important long-term complications of prepubertal cancer treatment [34]. According to statistics, the 5-year survival rate of childhood cancer can reach >85 %, and OTC is the only fertility preservation method for children [6]. Poirot et al. reported the world's first case of retransplanting cryopreserved ovarian tissue back into the body to induce puberty. Patients underwent cryopreserved ovarian tissue transplantation 27 months after hematopoietic stem cell transplantation (HSCT). Secondary sexual characteristics began to appear two months after transplantation and menarche appeared eight months after transplantation [35]. Since then, there have been many related reports of different diseases [36–38]. Current data show that the recovery rate, pregnancy rate and live birth rate of ovarian tissue cryopreservation before 18 years old are not lower than those undergoing cryopreservation after 18 years of age [39]. It is feasible for prepubertal girls to induce puberty and obtain fertility by OTCT. Data on the duration of induced puberty following OTCT are limited. There have been reports of transplantation of cryopreserved ovarian tissue in childhood and live births after pregnancy [37,40,41].

Recommendation 2–7: Cryopreserved ovarian tissue transplantation can be used to induce puberty development. (4, C).

3.5. Can pregnancy be obtained after transplantation of cryopreserved ovarian tissue?

There are differences in the pregnancy rates of OTCT in different ovarian tissue cryopreservation centers. A meta-analysis of 568 cases of post-OTCT fertility assessment showed a 37 % pregnancy rate after cryopreserved ovarian tissue transplantation [19]. However, the pregnancy rate of 53 cohorts in Denmark after OTCT was 56 % [42]. In 2021, China reported the first successful natural pregnancy and live birth after OTCT [43,44]. The FertiPROTEKT network reported on 244 transplants in 196 patients where 61.7 % of pregnant cases were natural pregnancies, and the pregnancy rate after transplantation decreased with the age of patients when ovarian tissue was cryopreserved [45].

Recommendation 2–8: Patients under 35 with good ovarian reserve have high pregnancy rates after OTCT. (2b, B).

4. Application of cryopreserved ovarian tissue transplantation

4.1. Can some patients with pelvic malignant tumours preserve ovarian function and fertility through ovarian tissue cryopreservation and transplantation?

Patients with early cervical squamous cell carcinoma have a low risk of ovarian metastasis, so patients with cervical cancer are less likely to recur after OTCT. According to the data from the first ovarian tissue cryobank in China, cervical cancer accounts for 49.31 % of OTC cases [46]; half the cases undergoing OTCT are patients with cervical cancer [32]. Cervical cancer accounts for about 61 % of gynecological tumour patients receiving OTC worldwide [20]. OTCT can help cervical cancer patients restore ovarian endocrine function, but successful pregnancy depends on whether the uterus is preserved and the degree of uterus damage caused by radiotherapy and chemotherapy [32].

OTCT can also be considered for patients with early and low-risk endometrial cancer. There have been cases of OTCT for patients with endometrial cancer, which have successfully restored ovarian endocrine function, and there are no reports of tumour recurrence [32].

When patients with ovarian tumours choose OTCT, it is necessary to evaluate the type, grade and stage of tumours and exclude the possibility of ovarian tissue carrying cancer. It is generally believed that ovarian cancer is a contraindication to OTCT. However, in 2015, Dittrich et al. reported a pregnancy and live birth case after OTCT in a patient with stage IIIc G1 ovarian serous adenocarcinoma and removed the transplanted ovarian tissue six weeks after delivery [47].

For other pelvic malignant tumours, such as rectal cancer and bladder cancer patients, the pelvic radiotherapy dose for rectal cancer patients is usually at least 45 Gy, and the pelvic 2 Gy radiotherapy dose can cause 50 % follicle death. Therefore, ovarian tissue should be biopsied and cryopreserved before radiotherapy to preserve ovarian function and fertility [48]. The first ovarian tissue cryobank in China reported on a patient with rectal cancer whose ovarian endocrine function is still good four years after transplantation of cryopreserved ovarian tissue [32].

Recommended 3–1: OTCT be used to restore ovarian function and fertility in patients with pelvic malignant tumours. (4, C).

4.2. Can patients with endometriosis preserve ovarian function and fertility through ovarian tissue cryopreservation and transplantation?

Patients with severe and recurrent ovarian endometriosis have been proven to have impaired ovarian reserve after surgery [49]. At the same time as endometriosis surgery, the healthy ovarian tissue cortex that has not been affected is cryopreserved and can be transplanted back into the body after the patient's disease is cured if the ovarian function is damaged. This provides a more promising choice for the fertility and ovarian function preservation of patients with endometriosis. It has been reported that this technology has been used to restore ovarian endocrine function and pregnancy [50–53].

Recommendation 3–2: Ovarian endometriosis and its surgical treatment will seriously affect ovarian function, and unaffected normal ovarian tissue can be cryopreserved at the time of surgery, which can preserve ovarian function and fertility. (3c, B).

4.3. Can breast cancer patients preserve ovarian function and fertility through ovarian tissue cryopreservation and transplantation?

Breast cancer is one of the best indications of OTCT. Among 2475 OTC patients reported in 2023, breast cancer accounted for 53 % [54]. Histological evaluation of 94 breast cancer patients undergoing OTC showed that follicular activity and density were similar in fresh and frozen-thawed ovarian tissues, and no micrometastases were found in ovarian tissues [55]. After thawing and transplantation of cryopreserved ovarian tissue, the recovery rate of ovarian function is over 95 % [56], and the cumulative live birth rate is about 40 % [57].

The timing of choosing OTCT for breast cancer patients should be determined so that the disease is at a low risk of recurrence and the patient has completed anti-tumour treatment for at least 3–6 months. For breast cancer patients with low recurrence risk who require adjuvant endocrine therapy, after multi-disciplinary evaluation, fully communicating the tumour risk and reproductive needs with patients, and receiving endocrine therapy for at least 2–3 years, they can carefully choose pregnancy after ovarian tissue transplantation. However, it is strongly recommended that they continue to complete endocrine therapy after delivery [58,59].

Recommendation 3–3: Young breast cancer patients can preserve ovarian function and fertility by ovarian tissue cryopreservation and transplantation. (4, C).

4.4. How to preserve the fertility of hematopoietic stem cell transplantation patients?

HSCT is widely used to treat leukemia, lymphoma, and immune diseases with HSCT indications (pigmented villonodular synovitis, dermatomyositis, hyperimmunoglobulin E syndrome, chronic active Epstein-Barr virus infection, etc.), metabolic diseases (mucopolysaccharide storage disease, galactosialic acid storage disease, pyruvate kinase deficiency anemia, mucolipid storage disease, metachromatic leukodystrophy, Niemann-Peak disease, etc.), non-malignant hematological diseases (aplastic anemia, myelodysplastic syndrome, thalassemia, Fanconi anemia, congenital dyserythropoietic anemia, congenital neutropenia, platelet dysfunction). In addition to non-solid tumours, HSCT is also applied to malignant solid tumours such as nephroblastoma and neuroblastoma [60]. However, HSCT can lead to severe iatrogenic POI, and the incidence rate can be as high as 93 % [61,62]. Therefore, all HSCT children and female patients of reproductive age should be provided with a timely fertility preservation consultation. Even after receiving HSCT during childhood, ovarian function and fertility should be evaluated and appropriate intervention should be given to increase the chances of future fertility and reduce the harm of early occurrence of various chronic diseases related to POI [60,63].

Recommendation 3–4: HSCT can lead to iatrogenic POI, and ovarian tissue cryopreservation and transplantation is the first choice to preserve ovarian function and fertility in such patients. (3c, B).

5. Construction of fertility preservation network

5.1. Why does cryopreservation of ovarian tissue suggest centralization?

OTCT technology is difficult, advanced and innovative. Centers with >10 cases of ovarian tissue transplantation are considered large centers, but there are only over 20 large ovarian tissue cryopreservation centers worldwide [19]. According to international guidelines, ovarian tissue cryopreservation should be centralized to ensure strict and high-standard quality assurance and management, safety and effectiveness. That is, ovarian tissue sampling surgery can be carried out in various places, and the biopsied ovarian tissue can be transported to the cryobank center for cryopreservation and storage [11,64]. For example, the FertiPROTEKT Fertility Preservation Network in Europe [43,65,66] and the American Cancer Fertility Alliance [67,68]. In 2012, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, established China's first ovarian tissue cryobank. Fifty-two medical units have participated in the fertility preservation of China's first clinical ovarian tissue cryobank.

Recommendation 4–1: Ovarian tissue cryopreservation should be centralized. (2b, B).

5.2. Is it feasible to build a wide-area fertility preservation network?

The application of high-tech equipment and standardized process to provide high-quality and high-standard cryopreservation, quality inspection and long-term storage of ovarian tissue for patients all over the country, to ensure a high success rate after thawing and transplantation, and to realize the recovery of ovarian endocrine function has been proved to be effective and feasible [69]. Low-temperature transport method at 4–8 °C is widely used for organ preservation and transport. Low-temperature delays cell metabolism and reduces cell oxygen demand and consumption [70]. In 2018, the European FertiPROTEKT Fertility Preservation Network pointed out that ovarian tissue should be remotely transported to the ovarian tissue cryobank center within 24 h using a 4–8 °C transport box [71].

Recommendation 4–2: Fresh ovarian tissue is transported at 4–8 °C for 24 h, which has no effect on follicular activity, and remote transportation is feasible. (4, C).

See the following table for all recommended items in this practice guideline:

Recommended content	Quality of evidence	Recommended strength
1. Ovarian tissue cryopreservation		
Recommendation 1–1: Ovarian tissue cryopreservation is suitable for preserving ovarian function and fertility in patients with tumour and non-tumour diseases and is the only preservation method of ovarian function and fertility for prepubertal girls and women of reproductive age who cannot delay ovarian toxicity treatment.	**2b**	**B**
Recommendation 1–2: Chemotherapy before OTC should not be considered a contraindication to ovarian tissue cryopreservation.	**2b**	**B**
Recommendation 1–3: Ischemia, mechanical injury and thermal injury must be avoided during ovarian tissue biopsy.	**1c**	**A**
Recommendation 1–4: Slow-freezing is the standard method of ovarian tissue cryopreservation, and vitrification of ovarian tissue is still a clinical study.	**1a**	**A**
2. Ovarian tissue transplantation		

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(*continued*)

Recommended content	Quality of evidence	Recommended strength
Recommendation 2–1: The risk of recurrence of primary disease after cryopreserved ovarian tissue transplantation is very low.	**3b**	**B**
Recommendation 2–2: Safety assessment of tumour contamination should be carried out before cryopreserved ovarian tissue transplantation.	**3b**	**B**
Recommendation 2–3: For patients with a high risk of cryopreserved ovarian tissue transplantation, such as leukemia, cryopreservation of ovarian tissue after chemotherapy to complete remission can reduce the risk of cryopreserved ovarian tissue transplantation.	**4**	**C**
Recommendation 2–4: Ovarian tissue transplantation should be considered at least 3–6 months after completion of radiotherapy and chemotherapy are finished for tumour patients.	**2b**	**B**
Recommendation 2–5: The timing of ovarian tissue transplantation should be decided after a multi-disciplinary consultation.	**4**	**C**
Recommendation 2–6: Cryopreserved ovarian tissue transplantation can restore ovarian function.	**2b**	**B**
Recommendation 2–7: Cryopreserved ovarian tissue transplantation can be used to induce puberty development.	**4**	**C**
Recommendation 2–8: Patients under 35 years of age with good ovarian reserve have high pregnancy rates after OTCT.	**2b**	**B**
3. The application of ovarian tissue cryopreservation transplantation in diseases		
Recommendation 3–1: OTCT be used to restore ovarian function and fertility in patients with pelvic malignant tumours.	**4**	**C**
Recommendation 3–2: Ovarian endometriosis and its surgical treatment will seriously affect ovarian function, and unaffected normal ovarian tissue can be cryopreserved at the time of surgery, which can preserve ovarian function and fertility.	**3c**	**B**
Recommendation 3–3: Young breast cancer patients can have their ovarian function and fertility preserved by ovarian tissue cryopreservation and transplantation.	**4**	**C**
Recommendation 3–4: HSCT can lead to iatrogenic POI, and ovarian tissue cryopreservation and transplantation is the first choice to preserve ovarian function and fertility in such patients.	**3c**	**B**
4. Construction of a fertility preservation network		
Recommendation 4–1: Ovarian tissue cryopreservation should be centralized.	**2b**	**B**
Recommendation 4–2: Fresh ovarian tissue is transported at 4–8 °C for 24 h, which has no effect on follicular activity, and remote transportation is feasible.	**4**	**C**

6. Discussion

This practice guideline consists of questions and recommendations, with 14 clinical questions and 18 recommendations, written by a multi-disciplinary team of gynecologists, fertility specialists, oncologists, reproductive medicine doctors and scientists. For patients, the risks and benefits of fertility preservation interventions require multi-disciplinary discussion and decision-making, and it is essential to provide patients with appropriate information and support their decisions.

OTCT is the most effective and promising method to protect ovarian function and fertility. Multi-disciplinary experts have been organized to develop this practice guideline to better guide the clinical application of OTCT technology in preventing and treating iatrogenic POI. Although the guidelines are generally limited, and the evidence supporting the current guidelines is also limited, the expert group believes that the guidelines will contribute to the best practices of OTCT in preventing and treating iatrogenic POI.

Contributors

Xiangyan Ruan contributed to the conception and design of the idea, coordination, and manuscript preparation and editing and was a member of the Expert Panel.

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All authors participated in preparing the practice guidelines and approved the final version of the manuscript.

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Declaration of competing interest

All members of the expert group declare that there is no conflict of interest.

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