A Survey Study of Attitude and Knowledge Regarding Female Fertility Preservation Among Reproductive Health Professionals in Fujian, China

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Purpose: Oncofertility is a newly developed medical field dedicated to preserving adolescent and young adult-aged cancer patients' fertility. For female cancer patients who desire to have children, fertility preservation has become an important concern before the cancer therapy. This study for the first time aimed to investigate attitude and knowledge regarding female fertility preservation among reproductive health professionals in China.

Methods: An online questionnaire assessing participants' demographics, experience, attitude, and basic knowledge regarding oncofertility was designed and distributed to reproductive health professionals in Fujian, one of the major regions for cancer and reproductive care in southeast China.

Results: The majority of participants (96.6%) who were familiar with fertility preservation were willing to collaborate with oncologists on preserving patients' fertility. However, ~20% of participants were not familiar with the term fertility preservation, and 30.4% and 52.2% of them were never consulted by a cancer patient or an oncologist about the infertility risk from cancer therapy, respectively. Years of working experience, but not gender, educational background, and marital status, was significantly associated with participants' oncofertility experience and attitude. A majority of participants (79.3%) had a middle or low level of oncofertility knowledge, which was significantly linked to their educational background.

Conclusion: Most of the surveyed reproductive health professionals held a positive attitude toward interdisciplinary collaboration with oncologists during oncofertility practice. However, the lack of their oncofertility knowledge highlighted the need of standard oncofertility education and training in China.

Keywords: oncofertility, cancer therapy, female fertility preservation, Chinese reproductive health professional

Introduction

THE PRODIGIOUS RISE IN CANCER SURVIVAL RATES over the past several decades has increased awareness on post-cancer quality of life.^{1,2} Infertility is one of the major off-target effects for both adolescent and young adult-aged (AYA-aged) female cancer patients.^{3,4} It is well acknowledged that anticancer treatments including both chemotherapy and radiation have highly detrimental effects on the ovaries, and can lead to the depletion of ovarian reserve, premature menopause, and infertility.^{5–7} Therefore, young female cancer patients tend to seek fertility preservation before cancer therapy. The term oncofertility was coined in 2006, de-

scribing this new discipline that focuses on preserving future fertility for AYA-aged cancer patients.^{8,9} Currently, cryopreservation of oocytes or embryos is available for reproductive-aged women, and cryopreservation of ovarian tissues and *in vitro* matured oocytes are options for prepubertal girls.^{10,11}

The American Society for Reproductive Medicine (ASRM) and American Society of Clinical Oncology (ASCO) in the United States and the Japan Society of Clinical Oncology (JSCO) recommend that cancer patients receiving gonadotoxic treatments should be informed of infertility risk and fertility preservation options, and a multidisciplinary collaboration of relevant medical specialists is encouraged.^{3,12,13} Although

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fertility preservation techniques have been developed for decades, it is still a challenge to choose an optimal option because patients have various ages, marital statuses, cancer types and locations, and urgencies of cancer therapy.^{10,14} Furthermore, the lack of fertility preservation knowledge, low efficiency of referring cancer patients to fertility specialists, and deficient communication between oncologists and fertility specialists add complexity for both patients and clinicians in oncofertility practice.¹⁰

Cancer has become a major public health issue in China.¹⁵ Approximately 3.8 million new cancer cases were diagnosed in China in 2014, including ~400,000 adults within their reproductive age and 22,400 childhood cancer patients.^{16,17} Meanwhile, 74% of young cancer patients had a desire to have children after cancer,¹⁸ and the improved cancer survival rate makes increasing cancer patients tend to preserve their fertility for future pregnancy.¹⁵ Although the assisted reproductive technologies (ARTs) such as *in vitro* fertilization (IVF) have been applied in China for >30 years, the fertility preservation service for patients with cancer is still limited due to the fact that oncofertility practice has yet to be integrated into the medical field or required by the laws and regulations. For instance, the fertility protective strategies commonly used in the United States and other western countries such as gonadotropin-releasing hormone agonist (GnRHa) treatment are not highly applied in China.^{19,20} Furthermore, surrogacy and oocyte donation are not made available by law in China.

Reproductive health professionals play critical roles in oncofertility practice, including communicating with oncologists and patients to discuss fertility preservation options and providing professional services.²¹ Compared with males, female fertility preservation is more complex, and it has been reported that the male cancer patients are about five times more likely to make arrangements for fertility preservation than females.²² As one of the major regions for cancer and reproductive care in southeast China, Fujian has a relatively high cancer incidence rate and a substantial number of young breast cancer patients.²³ Therefore, the objective of this study was to focus on fertility preservation for females, and to investigate the oncofertility attitude and knowledge of medical professionals in the field of female reproductive health in Fujian, China.

Materials and Methods

Participants and study area

An online questionnaire was distributed through WeChat, a Chinese social media platform, to the reproductive health professionals in the Department of Obstetrics and Gynecology (OBGYN) of hospitals in Fujian, China between August 1st and November 1st in 2017. Of 192 questionnaires submitted, 184 (95.8%) subjects were eligible for the study. Inclusion criteria were medical professionals in the field of female reproductive health, including obstetricians, gynecologists, fertility specialists, and nurses. All data were collected anonymously, and the submitted questionnaires were administered by Wenjuan, an online survey tool (wenjuan.com). The study was reviewed, and received an exemption from Human Research Subject Regulations by the Institutional Review Board (IRB) at the University of South Carolina in the United States and the First Affiliated Hospital of Xiamen University in China.

Questionnaire design

The questionnaire was designed to assess the demographics (questions 1–10), oncofertility experience and attitude (questions 11–21), and oncofertility knowledge (question 22) of the participants, and was translated from English to Mandarin (Supplementary Data). The questionnaire design and translation team was comprised of professional experts in the fields of reproductive medicine, oncofertility, reproductive biology, and public health, and all translators were bilingual in English and Mandarin to ensure accuracy and consistency. The question 22 included 12 true/false subquestions assessing participants' oncofertility knowledge. These questions were modified based on a previous study from Balthazar et al.²⁴ Each correctly answered question contributed 1 point to the total score. Based on each participant's total score, the oncofertility knowledge was categorized into three levels: 0–4 (low), 5–8 (middle), and 9–12 (high). To avoid uncertainty and bias in the data analysis of some questions, participants who were never consulted about infertility in question 11 were excluded in question 12 that asked the infertility consultation frequency; because the unfamiliarity to fertility preservation will cause uncertainty on answering whether participants' hospitals provided the fertility preservation service, those who reported "No" in the question 14 were excluded in the data analysis of question 15; participants who reported to be unfamiliar with fertility preservation in question 14 were also excluded in question 19 that asked the willingness on collaborating with oncologists on preserving patients' fertility; and participants who considered psychological counseling as unimportant in question 20 were excluded in question 21 that asked whether their hospitals provided the related services.

Statistical analyses

Descriptive statistics were performed by frequencies and percentage, and Spearman's rank correlation was assessed between demographic factors. Binary logistic regression models were used to predict the influence of demographic characteristics on participants' experience and attitude. To determine the impact of demographic factors on fertility preservation knowledge, an ordinal logistic regression model was applied. The Hosmer–Lemeshow test and the parallel lines test were used to evaluate the suitability of binary and ordinal logistic regression models, respectively. The level of significance was set at 0.05, and all the data analyses were conducted by SPSS 18.0 (SPSS, Inc., Chicago, IL).

Results

Demographic characteristics of participants

The demographic information of all 184 participants is described in Table 1. Approximately 90% of participants were female, which was consistent with the overall gender ratio in OBGYN departments in China.²⁵ The majority of participants were married (84.2%) and in their 30s or 40s (72.2%). More than half of them had at least one child (78.8%), had a bachelor's or higher educational degree (91.3%), worked in level 3-A hospitals (68.5%), and had >10 years of working experience (59.2%).

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF 184 ELIGIBLE PARTICIPANTS

Demographics	N (%)
Gender	
Male	19 (10.3)
Female	165 (89.7)
Age	
20–30	39 (21.2)
30–40	77 (41.8)
40–50	56 (30.4)
>50	12 (6.5)
Educational background	
High school diploma	16 (8.7)
Bachelor's degree	102 (55.4)
Master's degree	54 (29.3)
MD	12 (6.5)
Marital status	
Married	155 (84.2)
Unmarried	29 (15.8)
No. of children	
0	39 (21.2)
1	114 (62.0)
2	30 (16.3)
≥3	1 (0.5)
Hospital level	
Level 3-A	126 (68.5)
Level 3-B	19 (10.3)
Level 2-A	30 (16.3)
≤Level 2-B	9 (4.9)
Specialty	
Obstetrics	29 (15.8)
Gynecology	71 (38.6)
OBGYN	68 (37.0)
IVF	16 (8.7)
Years of working experience	
1–10	75 (40.8)
11–20	60 (32.6)
21–30	42 (22.8)
>30	7 (3.8)

IVF, *in vitro* fertilization; OBGYN, obstetrics and gynecology.

Questions of oncofertility experience and attitude

Table 2 lists the results of participants' oncofertility experience and attitude. A majority of participants (96.2%) have been consulted by patients about their infertility concern, and 74.0% of them encountered patients with infertility on a daily or weekly frequency. Approximately 70% of participants reported that they had been consulted by a female cancer patient about infertility concern from cancer therapy, and ~48% of them have been consulted by an oncologist about patients' infertility risk after cancer. Although 98.4% of participants reported knowing that chemotherapy or radiation can damage female fertility, 19.6% of them were not familiar with the term "fertility preservation."

With respect to the question of whether participants' hospitals provided fertility preservation services, 20.7% of them reported "Yes" and all of them were from the level 3 hospitals. This is consistent with the Chinese Medical Institution Regulations, which requires that only the level 3 hospitals are eligible to provide ART service.²⁶ Moreover, 97.8% of participants agreed that patients with cancer would

TABLE 2. QUESTIONS OF ONCOFERTILITY EXPERIENCE AND ATTITUDE

Questions	N (%)
Have you ever been consulted about infertility by patients?	
Yes	177 (96.2)
No	7 (3.8)
How often do you encounter patients with infertility?	
Daily	48 (27.1)
Weekly	83 (46.9)
Monthly	29 (16.4)
Yearly	17 (9.6)
Did you know that chemotherapy and/or radiation can damage female patients' reproductive functions, such as ovarian failure, early menopause, and even infertility?	
Yes	181 (98.4)
No	3 (1.6)
Are you familiar with fertility preservation, such as oocyte/embryo cryopreservation and ovarian tissue cryopreservation?	
Yes	148 (80.4)
No	36 (19.6)
Does your hospital provide fertility preservation services for female cancer patients?	
Yes	38 (20.7)
No	110 (59.8)
No answer	36 (19.6)
Do you think that cancer patients would want to preserve their fertility?	
Yes	180 (97.8)
No	4 (2.2)
Has a female cancer patient ever consulted with you about the fertility preservation for herself?	
Yes	128 (69.6)
No	56 (30.4)
Has an oncologist ever consulted with you about a patient's fertility?	
Yes	88 (47.8)
No	96 (52.2)
Are you willing to collaborate with oncologists to help young female cancer patients for fertility preservation?	
Yes	143 (96.6)
No	5 (3.4)
Is it important to provide psychological counseling to cancer patients who have a risk of infertility before or during cancer treatment?	
Yes	179 (97.3)
No	5 (2.7)
Does your hospital have doctors/specialists available to provide the psychological counseling for patients on fertility concern from anticancer treatment as well as options for fertility preservation?	
Yes	86 (46.7)
No	93 (50.5)
No answer	5 (2.7)

want to preserve their fertility, and 96.6% of those who were familiar with fertility preservation reported to be willing to collaborate with oncologists on preserving patients' fertility. When participants were asked about the psychological consultation during oncofertility practice, 97.3% of them agreed on its importance; however, 50.5% of their working hospitals did not offer this service.

Binary logistic regression analysis was utilized to predict the impact of demographic characteristics on participants' oncofertility experience and attitude. Before the model building, Spearman's rank correlation analysis was performed to detect the collinearity between demographic variables. Results showed that the age and marital status were significantly correlated with the years of working experience ($r=0.841$, $p<0.01$) and the number of children ($r=0.682$, $p<0.01$), respectively. Therefore, age and the number of children were filtered, and gender, educational background, marital status, hospital level, and years of working experience were included as independent variables in the final models. The results of binary logistic regression analysis for three oncofertility experience and attitude questions are listed in Table 3. Gender, educational background, and hospital level had no significant impact on the replies of these three questions. Married participants were more likely to be consulted by patients regarding female fertility preservation. The years of working experience had a significant impact on all three questions. Compared with participants with 1–10 and 21–30 years of working experience, the group of 11–20 years were more likely to know about fertility preservation. Similarly, the participants with 11–20 years were more likely to be consulted about patients' fertility by an oncologist than those who worked for <10 years. With respect to the question assessing whether they were consulted by female cancer patients on infertility risk after cancer, the possibility increased along with the years of working experience, except the group of >30 years.

Oncofertility knowledge questions

A majority of participants (72.8%) had a middle level of oncofertility knowledge, and 6.5% of them received scores indicating a low level. Table 4 lists all the knowledge questions and the correct rate for each question. Approximately 90% of participants were aware that frozen eggs/embryos cannot guarantee future pregnancy, and 89.7% of them correctly realized that methods for fertility preservation should be adjusted after anticancer treatment. However, 89.1% of participants held a wrong view that the risk of birth defects in future children would increase with chemotherapy treatments, and 87% of them incorrectly reported that IVF with embryo cryopreservation can only be used in patients without cancer.

An ordinal logistic regression model was performed to predict the impact of demographic factors on participants' oncofertility knowledge levels. Results showed that gender, marital status, hospital level, and years of working experience had no significant impact. However, participants with a high school diploma tended to obtain a lower level of oncofertility knowledge than those who had higher educational background ($p<0.01$).

Discussion

The significant advances in early cancer detection and anticancer regimen result in greatly improved cancer survivorship worldwide, including China. It is estimated that 36.9% of cancer patients in China will survive for at least 5 years after diagnosis.¹⁵ Among these individuals, a great

TABLE 3. THE RESULTS OF BINARY LOGISTIC REGRESSION ANALYSES FOR EXPERIENTIAL QUESTIONS

	Q1	Q2	Q3
	<i>Familiarity with fertility preservation</i>	<i>Experience of being consulted by a patient</i>	<i>Experience of being consulted by an oncologist</i>
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gender (ref. = male)			
Female	0.63 (0.11–3.44)	1.10 (0.33–3.72)	1.71 (0.58–5.08)
Educational background (ref. = high school diploma)			
Bachelor's degree	0.49 (0.10–2.44)	0.24 (0.05–1.14)	0.88 (0.23–3.33)
Master's degree	2.59 (0.52–12.99)	0.55 (0.12–2.60)	1.41 (0.36–5.58)
PhD	0.99 (0.10–9.66)	0.59 (0.07–5.26)	3.58 (0.53–24.09)
Marital status (ref. = married)			
Unmarried	0.36 (0.12–1.11)	0.29 (0.11–0.78) ^a	0.51 (0.19–1.38)
Hospital level (ref. = level 3-A)			
Level 3-B	^a	1.23 (0.37–4.13)	1.93 (0.66–5.65)
Level 2-A	0.99 (0.31–3.18)	0.41 (0.15–1.09)	0.45 (0.18–1.13)
≤Level 2-B	2.04 (0.20–21.08)	2.65 (0.28–24.65)	1.23 (0.29–5.28)
Years of working experience (ref. = 1–10)			
11–20	6.31 (2.04–19.52) ^b	2.90 (1.17–7.22) ^a	3.26 (1.42–7.45) ^b
21–30	5.22 (1.50–18.19) ^b	4.35 (1.46–12.97) ^b	1.97 (0.80–4.84)
≥31	^c	0.22 (0.03–1.74)	1.46 (0.23–9.41)

Q1: Are you familiar with fertility preservation, such as oocyte/embryo cryopreservation and ovarian tissue cryopreservation?

Q2: Has a female cancer patient ever consulted with you about a patient's fertility?

Q3: Has an oncologist ever consulted with you about a patient's fertility?

^a $p \leq 0.05$.

^b $p \leq 0.01$.

^cWe were unable to calculate the value of OR because all the patients chose Yes in the group.

CI, confidence interval; OR, odds ratio.

TABLE 4. CORRECT ANSWERS AND CORRECT RATES OF 12 ONCOFERTILITY KNOWLEDGE QUESTIONS

<i>Oncofertility knowledge questions</i>	<i>Correct answer</i>	<i>Correct rate (%)</i>
(1) All cancer treatments result in infertility or premature menopause.	False	76.1
(2) A patient must have a spouse to pursue fertility preservation treatment.	True	18.5
(3) All fertility preservation treatments have similar success rates at achieving pregnancy.	False	84.8
(4) Insurance usually covers fertility preservation treatments.	False	78.8
(5) Fertility preservation methods are the same before and after cancer treatment.	False	89.7
(6) Women who utilize fertility preservation methods increase their risk of cancer recurrence in the future.	False	57.1
(7) Egg freezing and embryo freezing have the same chances of future pregnancy.	False	73.9
(8) A woman who freezes her eggs will have access to them whenever she is ready to use them in the future.	True	39.7
(9) Future pregnancy is guaranteed with frozen eggs.	False	93.5
(10) Future pregnancy is guaranteed with frozen embryos.	False	89.1
(11) IVF with embryo freezing is a treatment only used in patients without a cancer.	False	13.0
(12) The risk of birth defects in future children increases with chemotherapy treatments.	False	10.9

number of them are young females, and will seek pregnancy and childbirth after cancer.¹⁰ The urgent reproductive need from cancer survivors has generated a growing interest in providing oncofertility service, which requires a multidisciplinary coordination between oncologists and fertility specialists.²⁷ Previous studies were predominantly focused on the role of oncologists in oncofertility practice,^{28–31} while the fertility preservation consultation and service provided by reproductive health professionals are of equal importance. This study for the first time assessed the oncofertility attitude and knowledge among reproductive health professionals in China.

The prevalence of sub- or infertility among Chinese reproductive-aged women has been increased from 6.7% in 1988 to 25.0% in 2011,³² and the possible reasons include delayed child bearing, unhealthy lifestyle, and environmental pollution.³³ Consistently, up to 96% of female reproductive health professionals have been consulted by patients for their infertility concern in our study, and 74.0% of them encountered this problem at a daily or weekly basis, suggesting the severe infertility incidence in China. Regarding young female cancer patients, most of them face a high risk of infertility caused by gonadotoxic cancer therapy³³; however, there are few guidelines and regulations targeting this specific population in China.

Although the majority of surveyed participants understood the reproductive damage of cancer therapy, 20% of them were not familiar with fertility preservation, which is the most important option for protecting cancer patients' reproductive viability.³⁴ In China, only the level 3 hospitals are allowed to provide ART service, which accounts for only a small percentage (7.7%) of all hospitals nationwide.^{26,35} Since 21.2% of the participants in our study were from hospitals lower than level 3, the limited access to ART may lead to their unfamiliarity to fertility preservation. Most of the participants (97.8%) agreed that cancer patients would want to preserve their fertility before cancer therapy, and ~70% of them had been consulted about infertility concern by female cancer patients, suggesting that there is an urgent need for providing cancer patients with the fertility preservation consultation and service in China.

Approximately 96.6% of participants who reported to be familiar with fertility preservation displayed a desire to col-

laborate with oncologists on preserving female cancer patients' fertility. However, only half of them have been consulted by oncologists about their patients' infertility risk, indicating a lack of communication between oncologists and female reproductive health specialists. Similarly, a previous nationwide study in the United States found that most of the oncologists were willing to discuss patients' infertility risk from cancer therapy, but over half of them rarely referred their patients to the reproductive specialists.² The main barriers of the fertility preservation referral from oncologist to reproductive specialist could be the lack of time, knowledge deficiency, and concerns of poor cancer prognosis.²⁹ These results suggest that the high percentage of participants who are willing to help patients and collaborate with oncologists may not reflect their actual practice, and an effective medical guideline or regulation is desired to correct for this disparity. Most of the participants recognized the importance of psychological consultation during oncofertility practice; however, nearly half of their hospitals did not provide this service. Cancer patients face psychological distress from both cancer diagnosis and side effects from cancer therapy, including infertility. Moreover, the poor coordination between oncologists and fertility specialists further exacerbates their anxiety.³⁶ To address this issue, the use of patient navigator is a good way to discuss patients' infertility risks, offer psychological consultation, and provide with fertility preservation options to cancer patients.^{10,36} In addition, a standardized navigation training, evaluation, and execution protocol are necessary to ensure the high quality of oncofertility care in China.³⁷

According to the results from a previous study focusing on OBGYN fellows in the United States, only 4% of the study subjects considered their fertility preservation knowledge level as adequate, and 76% of them desired more related education in this field.²⁷ In our study, only 20.6% of participants obtained a score at a high level, suggesting a lack of oncofertility knowledge, which may result in an unsuitable oncofertility practice. The questions regarding the risk of birth defects after fertility preservation and the potential of IVF with embryo freezing as a fertility preservation method for cancer patients had the lowest correct rates. These facts indicate the need for more oncofertility training and education for reproductive

health professionals, such as the Oncofertility Consortium and Korean National Fertility Preservation Network, which are nationwide networks in the United States and Korea, respectively, and provide educational and technical support to the regional hospitals, including lectures, hands-on workshops, and consultation.^{8,38}

When considering the impact of demographic characteristics on participants' oncofertility attitude and knowledge, it was found that participants with 11–20 years of working experience were more likely to be familiar with fertility preservation compared with participants with <10 years, suggesting that more years of working experience will enable female reproductive health professionals to obtain more oncofertility knowledge. It is surprising that participants with >20 and 30 years of working experience reported to know less about fertility preservation compared with participants with 11–20 years. This difference may reflect the development of fertility preservation in China. The application of germ cell cryopreservation started in the late 1980s in China, and it was then developed rapidly in the past two decades.¹⁷ Therefore, the reproductive health professionals with 10–20 years of working experience may have more exposure opportunities on learning the fertility preservation knowledge and techniques. The significant impact of educational background on participants' oncofertility knowledge scores suggests that the systemic medical training will enable reproductive health professionals to have a better understanding and knowledge on oncofertility practice.

There were several limitations in this study. The online questionnaire was distributed from one to another through WeChat platform, and those who finished the survey tended to have an inherent interest in oncofertility, potentially causing the selection bias. In addition, the questionnaire design can be further improved in future studies. For example, most of the participants were expected to answer “Yes” for question 13 when they generally knew the reproductive damage from cancer therapy. However, it is also possible that participants may answer “No” when they did not know the listed specific reproductive defects. Furthermore, our study was focused on the reproductive health professionals from only one province in China. Additional research is needed to broaden the scope to other areas in the country. Finally, the knowledge questions cited from a previous study by Balthazar et al.²⁴ were originally utilized to assess cancer patients' oncofertility knowledge. Whether it is suitable to apply this quantitative tool to reproductive health professionals is still unknown.

In conclusion, this study reveals that most of the surveyed Chinese reproductive health professionals have a positive attitude toward the interdisciplinary collaboration with oncologists; however, a lack of fertility preservation knowledge exists, which may hinder the oncofertility practice. These findings emphasize the need of a standard oncofertility education and training platform, and a rapid and effective navigation mechanism between oncologists, cancer patients, and reproductive health specialists.

Acknowledgments

The authors acknowledge the support of Arnold School of Public Health Start Up Fund to S.X., and Magellan Scholar Program to S.X. and M.K. in the University of South Carolina. In addition, this work was supported by the Center for

Reproductive Health After Disease (P50HD076188) from the National Institutes of Health National Center for Translational Research in Reproduction and Infertility (NCTRI). The study was reviewed and received an exemption from Human Research Subject Regulations by the IRB at the University of South Carolina in the United States and the First Affiliated Hospital of Xiamen University in China.

Author Disclosure Statement

No competing financial interests exist.

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