Current Practices toward Fertility Issues for Young Breast Cancer Patients: A Survey of the Korean Breast Cancer Society; The SMARTSHIP Study

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Purpose: This study aimed to investigate and analyze the current fertility-related practices for breast cancer patients; the results are intended to help improve the quality of life of young patients and survivors. **Methods:** This study collected voluntary responses to a questionnaire that was used to survey Korean breast cancer specialists. The questionnaire consisted of five categories: knowledge, practice behaviors regarding fertility preservation, barriers to discussing fertility preservation, attitude toward fertility issues, and demographics and medical background. **Results:** A total of 120 copies of the questionnaire were distributed; the response rate was 89%. The section of the questionnaire regarding knowledge indicated that most respondents had adequate fertility preservation knowledge for cancer patients. However, 13.1% of the respondents indicated that they thought pregnancy increased the cancer recurrence risk. Respondents' knowledge and attitudes about fertility preservation were not correlated with actual practice. The absence of patient's expressions (24.30%), high recurrence risk (27.10%), insufficient time in the clinic (21.50%), and hospital conditions such as no reproductive specialists or infertility clinic (16.82%), were considered major barriers to discussing fertility issues. **Conclusion:** Although more than 50% of the respondents thought that cancer treatment is more important than fertility preservation and it is complex and difficult, the Korean breast surgical oncologists were generally encouraging when discussing fertility issues with young breast cancer patients. Hence, breast clinicians should share with young patients the updated evidence regarding the feasibility and safety of pregnancy after cancer treatment and the available options so that the best decisions can be made.

Key Words: Breast neoplasms, Fertility preservation, Survivorship

INTRODUCTION

With cancer prognosis improvement due to treatment development, quality of life has become an important problem for cancer survivors. Infertility in young cancer survivors, especially if they were childless at the time of cancer diagnosis, may impose significant psychological distress and impaired quality of life in areas of emotional well-being, sexuality, and relationship [1]. The infertility risk with cancer treatments widely varies and is dependent on the patient's age as well as the

treatment types and combinations received [2].

In Korea, over 90% of breast cancer patients survive more than 5 years after the primary treatment including surgery [3]. Moreover, the breast cancer incidence among Korean patients in their 40s is higher than that in Western countries where the proportion of premenopausal breast cancer patients is very low. The proportion of patients younger than 40 years with breast cancer in Korea is approximately 13%. It is nearly two times higher than that in Western countries [4]. Breast cancer patients under age 40 years can achieve successful pregnancy and childbirth after treatment for breast cancer. Moreover, it is known that pregnancy itself does not increase the risk of breast cancer recurrence [5,6].

Currently, many countries have conducted research regarding fertility preservation in young cancer patients, and patient referral systems [7-9]. In addition, fertility counseling and maintenance before

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cancer treatment in patients with childhood cancer have shown to improve the quality of life after cancer treatment [10].

The practice of oncologists regarding fertility preservation for cancer patients of reproductive age may depend on multiple factors, such as patient's medical and psychosocial condition [11,12], patient's knowledge [13], and physicians' knowledge about fertility preservation [14].

However, at present, there are few studies on young breast cancer patients and survivors in Korea. Furthermore, most oncologists and patients tend to focus only on cancer treatment, and experience and knowledge of fertility preservation are not adequate. Particularly, young breast cancer patients and survivors' pregnancy are unfamiliar subjects.

The purpose of this study was to investigate and analyze the current fertility-related practices for breast cancer patients, and the results are intended to help improve the quality of life of young breast cancer patients and survivors.

METHODS

This study was conducted as a questionnaire survey obtaining voluntary response from the Korean Breast Cancer Society (KBCS) members. The questionnaire used in this study was a modified form of the questionnaire used in Japanese studies, with permission obtained from the author [15]. The modified questionnaire was reconfirmed by the Korean Breast Cancer Survivor study group. The questionnaire consisted of 45 questions in five categories, namely, knowledge, practice behaviors regarding fertility preservation, barriers to discussing fertility preservation, attitude toward fertility issue, demographic and medical background (Table 1). The respondents were asked to self-evaluate their agreement with the statements using a five-grade system (1. Strongly agree; 2. Agree; 3. Cannot decide; 4. Disagree; and 5. Strongly disagree). The questionnaire was distributed to the members of the Korean Breast Cancer Society who participated in the 2016 global breast cancer conference held at Jeju island. The questionnaire was distributed face-to-face and immediately collected after being answered. Approval for the study was obtained from our Institutional Review Board (IRB No. IS16QIS10054).

Statistical analysis

Data regarding demographic and specialty factors were summarized as frequencies and percentages. The chi-square test was used for correlation analysis between physician knowledge, attitude, and background. The Fisher's exact test was used when the frequency of each cell was less than 5. The odds ratios and their 95% confidence intervals were calculated using multivariate logistic regression analysis that examined the association between the fertility issues for young breast cancer patients and physician's fertility preservation knowledge, attitude, age, sex, religion, duration, institute, number of staff, genetic clinic, and number of operation per month, partner, children, and death of a neighbor. Data analysis was performed using STATA (version 15.0 StataCorp LP College Station, TX, USA); *p*-values less than 0.05 were considered to represent a statistically significant difference.

RESULTS

A total of 120 copies of the questionnaire were distributed, of which 107 questionnaires were answered, resulting in a response rate of 89%. Respondent demographics and characteristics are listed in Table 2. Of the respondents, 40 (37.4%) were women, 97 (90.7%) were breast surgeons, 6 (5.6%) were medical oncologists, and 4 (3.7%) were other specialty physicians.

Most respondents provided correct answers in the section regarding knowledge; the percentage of respondents who answered correctly ranged from 78% to 93%. However, 13.1% of the respondents indicated that pregnancy increased the recurrence risk, and 9.4% said they did not know if it increased cancer recurrence or not. Accuracy of knowledge about fertility was correlated with the number of staff where they worked ($p = 0.030$). The affiliated institution ($p = 0.040$) and the presence of a genetic counseling clinic ($p = 0.040$) were significantly correlated with a positive opinion toward fertility preservation for breast cancer patients (Table 3).

Respondents' knowledge and attitudes about the fertility preservation were not correlated with actual practice. Further, patients brought up the fertility issue more voluntarily with physicians who worked at university hospitals, who worked at institutes with more staff (≥ 4), and who had a spouse. The discussion frequency with patients about infertility due to cancer treatments was lower for physicians who worked at hospitals that performed more monthly surgeries. The pa-

Table 1. Questionnaire statements**A. Knowledge about fertility issues of breast cancer patients**

1. Total dose of alkylating agents are related to infertility
2. Pregnancy after breast cancer increases risk of recurrence
3. Pregnancy after chemotherapy increases risk of congenital anomaly
4. Pregnancy should be avoided during tamoxifen treatment
5. Luteinizing hormone releasing hormone (LHRH) analog reduces the risk of chemotherapy-induced amenorrhea
6. In the method of preserving the ability to be pregnant, what method do you know well?

B. Practice behavior

1. Patients voluntarily bring up the fertility issues in the clinic
2. I discuss the impact of cancer treatment to future fertility with my patients
3. I do not feel comfortable to discuss fertility issue with my patients
4. I take into account the history of childbirth when I discuss fertility issue with my patient
5. I take into account whether she has a spouse/partner when I discuss fertility issue with my patient
6. I take into account the economic status of the patient when I discuss fertility issue with my patient
7. I discuss fertility issues with breast cancer patients with high risk of recurrence
8. I refer patients who have questions about fertility to reproductive specialists
9. I provide my patients with educational material about fertility preservation
10. I use LHRH analog to preserve fertility reproductive specialists

C. Barriers for discussing fertility issues

1. The patient does not express their interest in fertility
2. The patient has high risk of recurrence
3. The patient has economic problems
4. The patient does not have a spouse/partner
5. There is no place/person to refer my patients to for fertility preservation
6. Time constraints affect my ability to discuss fertility preservation
7. What is the greatest difficulty in discussing fertility issues with young breast cancer patients?

D. Attitude toward fertility preservation

1. Patients with poor prognosis should not pursue fertility preservation
2. Treating cancer is more important than fertility preservation
3. Fertility preservation is difficult and complicated.
4. I fear passing hereditary cancer to a biological child
5. Losing mothers will negatively affect bereaved children

E. Demographics and medical backgrounds

1. What is your age?
2. What is your gender?
3. What is your religious background?
4. How long have you treated breast cancer patients?
5. What is your specialty?
6. What kind of institution do you practice in?
7. Where is your primary practice located?
8. How many breast surgeons are there in your practice setting including you?
9. Are there any female breast surgeon in your practice setting?
10. Are there any medical oncologists in your practice setting?
11. Are there any cancer-specialized pharmacists in your practice setting?
12. Is there a genetic counseling clinic in your practice setting?
13. In a month, how many breast cancer surgeries are performed in your practice setting?
14. In a month, how many breast cancer patients under 40 years of age do you see?
15. Do you have a spouse/partner?
16. Do you have children?
17. Do you have relatives or close friends who passed away leaving behind minor children?

tient's economic status was considered more by physicians who worked at hospitals with a large number of breast surgical oncologists.

In case of patients with a high relapse risk, breast surgeons with more than 10 years of clinical experience are more likely to discuss fertility

Table 2. Demographic backgrounds (n = 107)

Characteristic	No. (%)
Sex	
Male	67 (62.62)
Female	40 (37.38)
Age (yr)	
30-39	38 (35.51)
40-49	53 (49.53)
50-59	12 (11.21)
≥ 60	4 (3.74)
Religion	
Protestant	44 (41.12)
Catholic	27 (25.23)
Buddhist	4 (3.74)
Atheist	32 (29.91)
Career of breast cancer treatment (yr)	
< 5	8 (7.48)
5-10	26 (24.30)
11-15	31 (28.97)
16-20	30 (28.03)
> 20	12 (11.21)
Specialty	
Breast surgeon	97 (90.65)
Medical oncologist	6 (5.61)
Others	4 (3.74)
Type of affiliation	
University hospital	83 (77.57)
General hospital	18 (16.82)
Special hospital	3 (2.80)
Private clinic	3 (2.80)
Number of Breast surgeon	
1	11 (10.28)
2-3	45 (42.06)
4-5	21 (19.63)
≥ 6	30 (28.04)
Practice region	
Seoul	43 (40.19)
Gyeonggi	20 (18.69)
Gangwon	1 (0.93)
Chungcheong	10 (9.35)
Jeolla	17 (15.89)
Gyeongsang	15 (14.02)
Jeju	1 (0.93)
Female breast surgeon	
Present	73 (68.2)
Absent	34 (31.8)
Medical oncologist	
Present	96 (89.72)
Absent	11 (10.28)
Genetics clinic	
Present	57 (53.27)
Absent	50 (46.73)

(Continued to the next)

Table 2. Continued

Characteristic	No. (%)
No. of breast cancer surgeries (per month)	
1-10	18 (16.82)
11-50	58 (54.21)
51-100	9 (8.41)
> 100	22 (20.56)
No. of patients aged < 40 (per month)	
0-2	26 (24.30)
3-5	38 (35.51)
6-9	11 (10.28)
≥ 10	32 (29.90)
Partner/spouse	
Present	90 (84.11)
Absent	17 (15.89)
Children	
Present	87 (81.31)
Absent	20 (18.69)
Relatives/close friends who passed away leaving behind young children	
Present	29 (27.10)
Absent	78 (72.90)

issue. Respondents without a relative or a friend who died and left a child behind and respondents who had more than a decade of experience with breast cancer treatment referred more patients to reproductive specialists. Moreover, respondents who were religious, worked at a hospital with a genetic clinic, and did not have a relative or a friend who died and left a child behind provided patients with more informative materials about fertility preservation (Table 4).

The absence of patient's interest in fertility (24.30%), high risk of breast cancer recurrence (27.10%), insufficient time in the clinic (21.50%), and hospital settings such as no reproductive specialists or infertility clinic (16.82%) were regarded as major obstacles for fertility issue discussion (Table 5).

DISCUSSION

Recently published clinical practice guidelines by the American Society of Clinical Oncology and several other publications have highlighted fertility preservation and recommended offering fertility counseling to all young cancer patients before primary cancer treatment.

In the previous survey performed in Japan, almost one-third of the patients who expressed an interest in fertility selected a different adjuvant treatment than that treatment primarily recommended by the

Table 3. Demographic factors associated with knowledge and attitude for fertility preservation

Factor	Knowledge			Attitude		
	No knowledge	Knowledge	p-value	Unfavorable	Favorable	p-value
Age (yr)						
30-39	20	18	0.410*	12	26	0.310*
40-49	19	34		15	38	
50-59	5	7		4	8	
≥ 60	1	3		3	1	
Gender						
Male	19	21	0.380	13	27	0.900
Female	26	61		21	46	
Religion						
Protestant	16	28	0.620*	10	34	0.120*
Catholic	14	13		10	17	
Buddhist	2	2		0	4	
Atheist	13	19		14	18	
Career of breast cancer treatment (yr)						
≤ 5	6	2	0.310*	3	5	0.730*
6-10	11	15		8	18	
11-15	14	17		11	20	
16-20	10	20		7	23	
> 20	4	8		5	7	
Type of affiliation						
University hospital	32	51	0.470*	22	61	0.040*
General hospital	10	8		10	8	
Special hospital	1	2		1	2	
Private clinic	2	1		1	2	
Number of Breast surgeon						
1	5	6	0.030*	3	8	0.930*
2-3	23	22		16	29	
4-5	11	10		6	15	
≥ 6	6	24		9	21	
Genetics clinic						
Present	22	35	0.440	23	34	0.040
Absent	23	27		11	39	
No. of breast cancer surgeries (per month)						
0-10	10	7	0.170*	5	12	0.890*
11-20	13	17		8	22	
21-50	14	14		9	19	
51-100	3	6		4	5	
> 100	5	17		7	15	
Partner/spouse						
Present	36	54	0.320	27	63	0.360
Absent	9	8		7	10	
Children						
Present	35	52	0.430	26	61	0.380
Absent	10	10		8	12	
Relatives/close friends who passed away leaving behind young children						
Present	16	13	0.090	11	18	0.400
Absent	29	49		23	55	

*Fisher's exact test.

Table 4. Factors associated with fertility-related practice behavior

Variable	OR (95% CI)	p-value
B-1. Patients voluntarily bring up the fertility issues in the clinic	Institute University 1.00 hospital Others 0.21 (0.05-0.94)	0.040
	No. of staff 1-3 1.00 ≥ 4 17.82 (4.31-73.59)	< 0.001
	Partner Yes 1.00 No 2.00e-10 (3.72e ⁻¹¹ -1.07e ⁻⁰⁹)	< 0.001
B-2. I discuss the impact of cancer treatment to future fertility with my patients	No. of OP per month operation ≤ 10 1.00 11-100 0.12 (0.02-0.80) > 100 0.05 (0.01-0.62)	0.030 0.020
B-6. I take into account the economic status of the patient when I discuss fertility issue with my patient	No. of staff 1-3 1.00 ≥ 4 3.34 (1.09-10.24)	0.030
B-7. I discuss fertility issues with breast cancer patients with high risk of recurrence	Duration (yr) ≤ 10 1.00 11-20 4.96 (1.56-15.83) > 20 12.19	0.010 0.070
B-8. I refer patients who have questions about fertility to reproductive specialists	Duration (yr) ≤ 10 1.00 11-20 4.42 (1.29-15.18) > 20 8.79 Death of a neighbor Yes 1.00 No 4.23 (1.27-14.17)	0.020 0.110 0.020
B-9. I provide my patients with educational material about fertility preservation	Religion Yes 1.00 No 0.19 (0.06-0.60) Gene clinic Yes 1.00 No 0.32 (0.10-0.95) Death of a neighbor Yes 1.00 No 3.31 (1.05-10.48)	0.010 0.040 0.040

OR = odds ratio; CI = confidence interval; OP = operation.

oncologist because of their desire to preserve fertility [16]. Therefore, young Korean breast cancer patients may choose a different adjuvant therapy if appropriate information regarding fertility preservation is provided before breast cancer treatment.

The practice of oncologists regarding fertility preservation for can-

Table 5. Barriers for discussing fertility issues (n = 107)

Variable	No. (%)
The patient does not express their interest in fertility	26 (24.30)
The patient has high risk of recurrence	29 (27.10)
The patient has economic problems	7 (6.54)
The patient does not have a spouse/partner	4 (3.74)
There is no place/person to refer my patients to for fertility preservation	18 (16.82)
Time constraints affect my ability to discuss fertility preservation	23 (21.50)

cer patients of reproductive age may depend on multiple factors, such as patient's medical and psychosocial condition [11,12], patient's knowledge [13], and physicians' fertility preservation experience [14]. This is the first study to describe the knowledge, attitudes, and behavior of breast surgical oncologists toward fertility issues in young Korean breast cancer patients. Although a previous survey in the United States showed that many breast cancer clinicians reported that they do not have knowledge of/ or resources for fertility preservation [14], our results indicated that most respondents were well -aware of the current anti-cancer treatment impact on fertility and fertility preservation option such as oocyte cryopreservation, embryo cryopreservation, and ovarian tissue cryopreservation.

The present study showed that breast surgical oncologists generally had a positive attitude toward fertility preservation. The high response rate to this survey revealed the interest of KBCS members in fertility issue. A total of 89.7% (96/107) of the participants responded that they were positive in discussing fertility issue with young breast cancer patients. Although more than half of the respondents said that cancer treatment is more important than fertility preservation and that maintaining the ability to be pregnant is complicated and difficult, 40% of the respondents showed that they discussed issues related to childbearing with patients with high likelihood of relapse.

Results showed that 60% of the respondents always or often refer their patients to infertility specialists. This result was higher than in previous surveys performed in the United States (47%) and Japan (42%) [7,14]. However, these results indicate that 40% of breast surgical oncologists still do not refer patients to infertility specialists. The reason is not clear. However, 38% of the respondents answered that it is difficult for them to discuss fertility preservation because there are no fertility-related department or fertility experts at their hospitals.

Results of a study by Quinn et al. [6] showed that 47% of the re-

sponding oncologists often refer their patients to infertility specialists; however, these results indicate that more than half of the oncologists do not refer their patients. The likelihood of referring patients to infertility specialists was predicted by the sex and attitudes toward fertility preservation of oncologists. Female physicians are possibly more aware of patients' desire for family and information regarding fertility-related issues. Velikova et al. [17] performed a qualitative study of quality of life issues and found that female oncologists were more willing to discuss sexuality and felt that such discussions had high impact on the survivors' quality of life. However, there was no correlation in our study.

A high disease recurrence risk was considered the greatest barrier to discussing fertility for physicians, which was similar to the results of other studies [11,12]. When the patient had advanced breast cancer with a high likelihood of recurrence, both the patient and physician tended to refrain from discussing the future ability to achieve pregnancy. In this case, patient care should include not only referral to reproductive specialists but also informational, psychological, social, and religious (if applicable) support. Other reasons that were barriers to discussing fertility were patients not expressing an interest in fertility, insufficient medical consultation time, and hospital circumstances. Nevertheless, patients who did not voluntarily express an interest in fertility may have not known about the possibility of infertility due to cancer treatment or may have not known about fertility preservation. Therefore, if information had been provided about these issues, the results would have been different.

This study revealed that it is necessary to improve medical care by readjusting medical fees, increasing research regarding patient needs, and creating a system for patient referrals.

Forman et al. [18] showed that reluctance among physicians to discuss fertility preservation or to refer patients to fertility specialists is due to the associated costs. However, in our survey, only 6% of the respondents considered the patients' economic circumstances. This seemed to be because most patients in Korea have private insurance that pays for their medical costs.

This study was limited by the small sample size and patients not being surveyed. Further investigations of patients' needs are required because patients and physicians often have discordant perceptions of patients' needs and problems. Another limitation of this study is that the results from the surveys may be biased due to the diverse roles of a

breast surgical oncologist since each institution has their own different clinical practice, which may result in differences in the perceptions of fertility issues. This study will be meaningful as a study of the physician's view of young breast cancer patients from the initial breast cancer diagnosis to further treatment plans.

In conclusion, although more than 50% of the respondents believed that cancer treatment is more important than fertility preservation and that fertility preservation is complex and difficult, Korean breast surgical oncologists were generally positive when discussing fertility issues with young breast cancer patients. Breast clinicians should share with young patients the updated evidence regarding the feasibility and safety of pregnancy after cancer treatment and the available options for fertility preservation so that the best decisions can be made.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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