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Investigation of Fertility Preservation Education Videos for Pediatric Patients Based on International and Historical Survey

Yuriko Iwahata, MD,¹ Seido Takae, MD, PhD,¹ Hideyuki Iwahata, MD, PhD,¹ Kimikazu Matsumoto, MD, PhD,²
 Masahiro Hirayama, MD, PhD,³ Junko Takita, MD, PhD,⁴ Atsushi Manabe, MD, PhD,⁵ Yuko Cho, MD, PhD,⁵
 Tomoaki Ikeda, MD, PhD,⁶ Tadashi Maezawa, MD, PhD,⁶ Mitsuru Miyachi, MD, PhD,⁷ Dai Keino, MD, PhD,⁸
 Tomoe Koizumi, PhD,^{1,9} Tetsuya Mori, MD, PhD,¹⁰ Naoki Shimizu, MD, PhD,¹⁰
 Teresa K. Woodruff, PhD,¹¹ and Nao Suzuki, MD, PhD¹

Purpose: Recently, direct communication with children about cancer seems to have shifted, but little is known about communication regarding discussions of future infertility risk due to cancer therapy. This study conducted cross-cultural comparisons between Japan and the United States to clarify communication patterns about cancer notification and develop appropriate information about fertility issues.

Methods: An online survey was distributed to members of the Japanese Society of Pediatric Hematology/Oncology in July 2019 and the American Society of Pediatric Hematology/Oncology in July 2020. Based on the results from the survey, we developed three types of educational videos: a prepubertal version A, B, and a pubertal version. Next, we conducted a survey to assess whether these were appropriate for clinical practice.

Results: We analyzed 325 physicians in Japan and 46 in the United States. In Japan, 80.5%, 91.7%, and 92.1% of the physicians notified patients aged 7–9, 10–14, and 15–17 years of their cancer diagnosis directly, respectively, compared within the United States, where the rate was 100%, regardless of age. Further, 9% and 45% of physicians in Japan and the United States, respectively, discuss fertility issues directly with patients aged 7–9 years. In the survey to assess the educational videos, 85% of the physicians preferred to use the educational videos in clinical practice.

Conclusion: This is the first step in bringing concordance to communication patterns for emerging cancer care around the globe and that this study and its intervention arm provide guidance in ways that ensure global equity in care.

Keywords: adolescent, child, fertility preservation, oncofertility, pediatric, oncology

¹Department of Obstetrics and Gynecology, St. Marianna University School of Medicine, Kanagawa, Japan.

²National Center for Child Health and Development, Children's Cancer Center, Tokyo, Japan.

³Department of Pediatrics, Mie University Graduate School of Medicine, Tsu, Japan.

⁴Department of Pediatrics, Graduate School of Medicine, Kyoto University, Kyoto, Japan.

⁵Department of Pediatrics, Hokkaido University, Sapporo, Japan.

⁶Department of Obstetrics and Gynecology, Mie University, Tsu, Japan.

⁷Department of Pediatrics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan.

⁸Division of Hematology/Oncology, Kanagawa Children's Medical Center, Yokohama, Japan.

⁹International Center for Reproductive Medicine, Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan.

¹⁰Department of Pediatrics, St. Marianna University School of Medicine, Kanagawa, Japan.

¹¹Department of Obstetrics and Gynecology, Michigan State University, East Lansing, Michigan, USA.

Introduction

CANCER IS WIDELY recognized around the world as a life-threatening disease, and the numbers of patients with cancer, including those of childhood, adolescent, and young adult (CAYA) age, are increasing.¹ Consequently, 10% of patients with cancer experience infertility because of impaired gonadal function due to gonadotoxic cancer treatments (e.g., chemotherapy and radiation therapy). Moreover, sexual dysfunction after cancer and treatment is still under-recognized as a serious problem faced by cancer survivors.² Children with a history of cancer have expressed their desire for disclosing infertility risks at cancer diagnosis.^{3,4}

Fertility preservation (FP) treatment has been established to improve quality of life among adult cancer survivors. The Oncofertility Consortium and FertiPROTEKT are representative associations established in 2006 to promote FP, followed by the Japanese Society for Fertility Preservation (JSFP) in 2012.⁵ In prior research published in 2007, a survey comparing Japan and the United States regarding direct cancer diagnosis disclosure for childhood and adolescent patients with cancer found that 65% of physicians in the United States *always* informed patients of the diagnosis, compared with 9.5% in Japan,⁶ which revealed that most physicians in the United States feel that it is their responsibility.⁷

Since 2018, major societies such as the American Society of Clinical Oncology (ASCO), and the Japan Society of Clinical Oncology (JSCO) Clinical Practice Guidelines for Fertility Preservation in CAYA with Cancer^{8,9} have recommended that health care providers explain fertility issues to all patients of reproductive age, regardless of gender or age, and refer them to a reproductive medicine specialist before treatment.^{6,10,11} Particularly in Japan, FP for children is expected to increase as a result of the start of government subsidies for FP among patients with cancer in 2021. However, no current methodologies specify how information should be provided, and methods of providing information are currently left to each individual medical professional.¹² As a result, health care providers often find it difficult to provide information on FP, especially to pediatric patients. Therefore, less than half of pediatric patients have received explanations about fertility issues after cancer treatment, and in many cases, the patients are unaware of declining fertility.^{13,14}

Although some reports have described cancer diagnosis disclosure with children,⁶ to our knowledge, no studies have investigated communication between physicians and children about infertility risk at the time of a cancer diagnosis. Therefore, our clinical questions are as follows: (i) How have physicians' direct discussions involving informing pediatric patients about a cancer diagnosis shifted in the past 15 years, and are there any differences between Japan and the United States?; and (ii) What proportion of physicians provide information to patients with pediatric cancer at a cancer diagnosis in regard to fertility issues? We believe that answering these clinical questions could improve the frequency of information provision regarding fertility issues to patients with childhood and adolescent cancer.

Materials and Methods

The whole process of the study is shown in Figure 1. The survey was conducted in both Japan and the United States

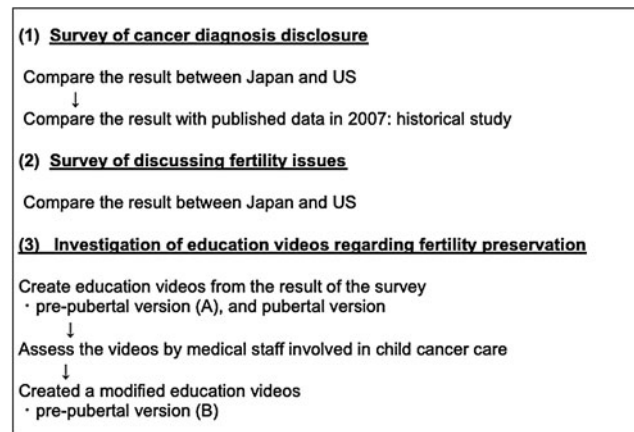


FIG. 1. Whole process of the study.

regarding cancer diagnosis disclosure and discussion fertility issues. From the result, we created education videos regarding FP for prepubertal and pubertal patients. Next, we assessed the videos, and since modifications are needed for prepubertal version, we created new version for prepubertal patients.

Questionnaire design and analysis

Questionnaires designed to evaluate physicians' perspectives regarding cancer diagnosis disclosure and information provision about fertility issues were distributed from July to September 2019 in Japan, and from July 2020 to March 2021 in the United States. The survey was developed in English based on an extensive review of literature, interviews with experts in pediatric oncology and survey methodologists in both the United States and Japan. The survey underwent review by clinical and survey experts in both countries to ensure that the instrument reflected culturally equivalent content.

The questionnaires were composed of 24 items, including five on demographics, six on cancer diagnosis disclosure, and 13 on fertility issues (Supplementary Data S1–S3). The six cancer diagnosis disclosure questions asked about the age limitations of patients when disclosing a cancer diagnosis, the factors influencing the physicians' timing of disclosure, and physicians' attitudes. To investigate the current state of cancer diagnosis disclosure and the age of the patients, we examined the disclosure rate by three age groups: prepubertal, beginning of puberty, and during puberty.

The 13 items on fertility issues asked about age limitations of patients when discussing the risk of gonadal dysfunction/future infertility with children and the factors influencing physicians when deciding to inform of the associated infertility risks. The answers regarding age limitations covered the same age range as those for cancer diagnosis disclosure (Supplementary Data S2).

The results were analyzed historically through a comparison with a 2007 study to analyze changes that had occurred for the past 15 years.

Questionnaire distribution and survey completion

In Japan, the questionnaires were distributed by email through sending a link to members of the Japanese Society of

Pediatric Hematology Oncology (JSPHO). Subsequently, the English version of the questionnaire was distributed through a post on the website of the American Society of Pediatric Hematology/Oncology (ASPHO). Then, more participants were recruited by email messages in which physicians who belonged to the Oncofertility Consortium in the United States and chief oncology physicians sent the link to the survey to their colleagues. The exclusion criteria are shown in Figure 2. All data were collected anonymously using Qualtrics online survey software (<http://qualtrics.com>).

Ethical considerations

This study was approved by the ethics review board of St. Marianna University School of Medicine (approval No. 3823, UMIN000048535). The study was reviewed and obtained an exemption from Human Research Subject Regulations by institutional review boards in the United States. All participants were informed that participation in the study was voluntary, and their identity would be kept confidential.

Historical study

The result was compared with prior research published in 2007 historically to investigate the 15-year trend of cancer diagnosis disclosure.

Statistical analysis

Qualtrics online survey software was used for all data entry and analyses. Descriptive data were shown as number (*n*), prevalence (%), mean, and standard deviation.

Creation of educational videos for FP

Based on the results from the survey, we developed two types of educational videos, which can be seen in Supplementary Data S4 and S5: a prepubertal version (A) and a pubertal version. Next, we conducted a survey to assess whether these were appropriate for clinical practice. Finally, we also created a new prepubertal video (B) (Supplementary Data S6) after hearing opinions from health care professionals. Prepubertal videos A and B are related to ovarian

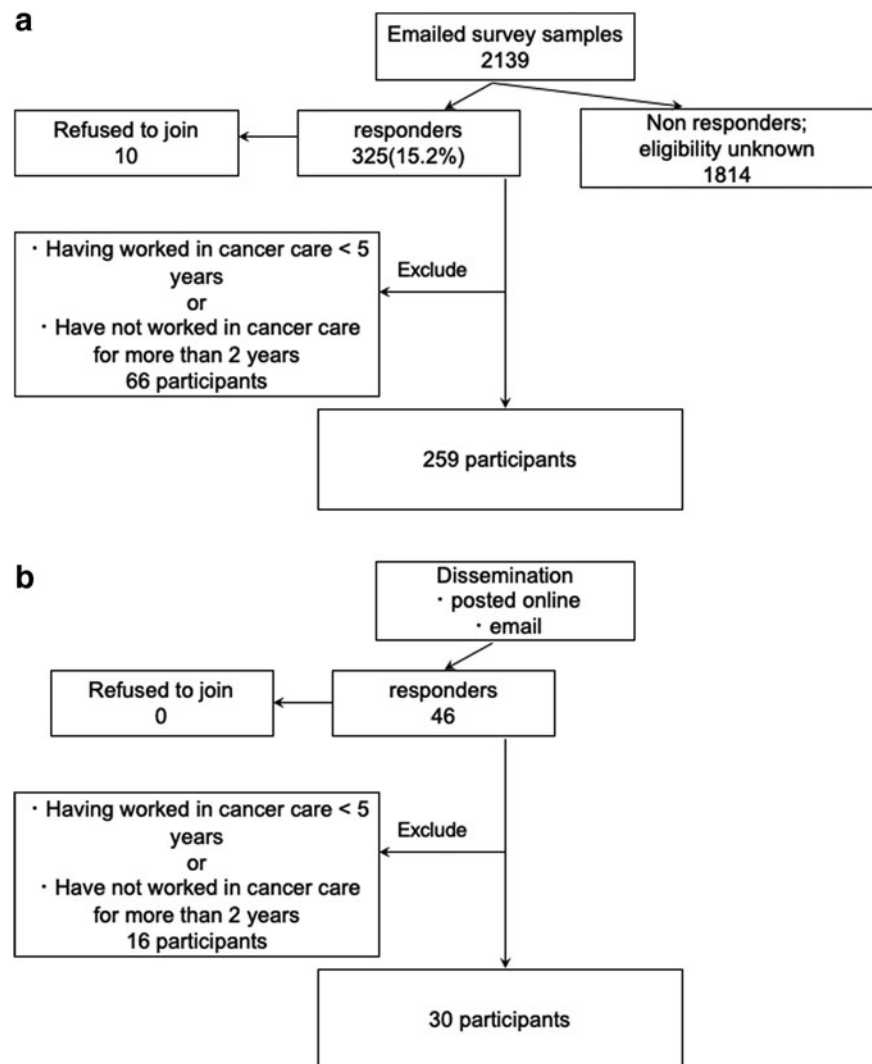


FIG. 2. Flow of research in Japan and the United States. **(a)** Survey response rate in Japan. **(b)** Survey response rate in the United States. The exclusion criteria are included in the figure.

TABLE 1. PARTICIPANT CHARACTERISTICS

Characteristics	N (%)	
	Japan	United States
Gender		
Male	226 (75.8)	10 (24.4)
Female	72 (24.2)	30 (73.2)
Prefer not to say	0	1 (2.4)
Years as physician		
<5	0	11 (26.8)
5–10	14 (4.7)	9 (22.0)
11–15	45 (15.1)	5 (12.2)
>15	239 (80.2)	16 (39.0)
Years of working in cancer care		
<5	12 (4)	10 (24.4)
5–10	39 (13)	9 (22.0)
11–15	36 (12)	2 (4.9)
>15	184 (61.7)	19 (46.3)
Have not worked in cancer cares for >2 years	26 (8.7)	1 (2.4)
Specialty		
Pediatric hematology/oncology	233 (78.2)	25 (60.9)
Pediatric surgery	35 (11.7)	3 (7.3)
Neurosurgery	6 (2)	0
Others	24 (8.05)	13 (31.7)
Working hospital		
University hospital	168 (56.4)	Freestanding children's hospital—Academic 22 (53.7)
Others	140 (43.6)	Children hospital within adult hospital—Academic 11 (26.3) Others 8 (19.4)

tissue cryopreservation (OTC) for patients with pediatric cancer, and the pubertal version includes general FP information on topics such as oocytes, embryos, and sperm cryopreservation for during and after puberty.

Results

Comparison between Japan and the United States

Survey responses. In Japan, a total of 325 of 2139 JSPHO members completed and submitted the survey. After

excluding incomplete responses, 259 (12%) valid questionnaires were eligible for analysis. In the United States, 46 participants responded to the survey, and after exclusions, 30 valid questionnaires remained (Fig. 2a, b). The response rate could not be calculated for the United States because the distribution was uncountable.

Characteristics of the participants. In Japan, the majority of physicians (75.8%) were male and 61.7% were experts in cancer care. The major specialty was pediatric hematology/oncology in both countries. In the United States, the majority of physicians were female (73.2%) and cancer care experience was nearly identical for each age group (Table 1).

Cancer diagnosis disclosure—a historical study. As shown in Table 2, 36% of Japanese physicians reported *always* directly disclosing a cancer diagnosis to children aged 7–9 years; an additional 32% reported *most of the time* (total 68%). By contrast, 60% of U.S. physicians reported *always* directly revealing and 40% *most of the time* (total 100%). Furthermore, regarding children over 15 years of age, >90% of the physicians in both countries directly revealed their cancer diagnosis. These results indicate that especially in Japan, patients around 7–9 years of age are sometimes considered to be too young to hear a cancer diagnosis directly.

As evidence to support this, as shown in Table 3, 72% of physicians in Japan cite the “age of the child” as a major influencing factor in cancer diagnosis disclosure. As with other factors, it was found that parental requests to disclose information and the possibility of cure hindered cancer diagnosis disclosure more often in Japan than in the United States. However, compared historically, cancer diagnosis disclosure for young children have become more common (38%–68% in Japan).

Discussing fertility issues. In Table 4, for patients aged 7–9 years, 7% of the physicians in Japan reported discussing fertility issues *before cancer treatment*, compared with 40% in the United States. Japanese physicians tended to tell only the parents before the start of cancer treatment. For patients aged 10–14 years, 41% of the physicians in Japan reported discussing fertility issues before the start of cancer treatment, compared with 85% in the United States. For patients aged 15–17 years, 75% of the physicians in Japan reported discussing fertility issues before the start of cancer treatment, compared with 95% in the United States. These results indicate that physicians tend to discuss fertility issues with child and adolescent patients as they become older. In Table 3, the results indicated that the “age of the child” and

TABLE 2. THE FREQUENCY TO TELL THE CANCER DIAGNOSIS DIRECTLY TO CHILD AND ADOLESCENT PATIENTS

	7–9 years		10–14 years		15–17 years	
	Japan	United States	Japan	United States	Japan	United States
Always	73 (35.8%)	12 (60%)	132 (64.7%)	18 (90.0%)	157 (77.0%)	19 (95.0%)
Most of the time	66 (32.4%)	8 (40%)	47 (23.0%)	2 (10.0%)	36 (17.7%)	1 (5%)
Some of the time	33 (16.2%)	0 (0%)	14 (6.9%)	0 (0%)	1 (0.5%)	0 (0%)
Rarely	17 (8.3%)	0 (0%)	2 (1.0%)	0 (0%)	0 (0%)	0 (0%)
Never	8 (3.9%)	0 (0%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)
Missing	55	10	55	10	55	10

TABLE 3. THE FACTORS INFLUENCE YOUR DECISION TO TELL “CANCER NOTIFICATION” AND “THE FERTILITY ISSUES”

<i>Cancer notification</i>			<i>The risk of gonadal dysfunction/future infertility</i>		
	<i>Japan</i>	<i>United States</i>		<i>Japan</i>	<i>United States</i>
Age of child	147 (72.1%)	9 (45.0%)	Age of child	184 (87.6%)	15 (75.0%)
Likelihood of cure	87 (42.7%)	1 (5.0%)	Parental understanding of the child situation	117 (55.7%)	9 (45.0%)
Parental request regarding how much information is shared	117 (57.4%)	7 (35.0%)	MD’s low confidence in knowledge of infertility risks for fertility issues	80 (38.1%)	1 (5.0%)
Parental understanding of the child situation	123 (60.3%)	7 (35.0%)	The physicians’ perception of the family’s ability to afford fees and storage	48 (22.9%)	0 (0%)
			Child’s sex	65 (31.0%)	1 (5.0%)
			Experimental method of FP (OTC/TTC)	63 (30.0%)	6 (30.0%)

OTC, ovarian tissue cryopreservation; TTC, testicular tissue cryopreservation.

“parental understanding of the child’s situation” can be communication barriers to fertility discussions (Table 5).

Educational videos. As >90% of physicians think that it is better to have explanatory material when explaining infertility risks, especially in Japan (Table 5), we developed education videos and conducted video assessment survey. The participants’ characteristics are shown in Supplementary Data S7. A hundred percent of participants responded that educational videos are necessary when discussing fertility issues (Supplementary Data S8). More than 80% of the physicians agreed that the pubertal version should be used in clinical practice; however, 38% of participants disagreed about the use of the prepubertal version, suggesting that some modifications are needed.

The dissenting opinions included sentiments such as “it is not a good idea to treat doctors as heroes,” “there are too many metaphors and it is difficult to convey specifically what you are trying to say,” and “the pictures are aggressive and can be frightening.” Therefore, we developed a new prepubertal version video (B), which can be seen in Supplementary Data S6. We again conducted a survey to assess this new version of the video, and the results are shown in Supplementary Data S9 and S10. In total, 85% of the physicians preferred to use the new version in clinical practice. Many

opinions about the new version were positive (e.g., “the pictures are gentle,” “the wording is specific and easy to understand”).

Discussion

Cancer diagnosis disclosure—a historical study

In this study, >60% of Japanese physicians disclosed a cancer diagnosis to pediatric patients aged 7–9 years directly, compared within the United States, where this rate was dramatically higher, at >90% regardless of age. The factors that influence physicians when notifying children of a cancer diagnosis were the “age of the child” and “parental understanding.”

The history of cancer diagnosis disclosure provides a deeper understand of their progression. According to a report in 1961, 90% (n = 197/219) of physicians in the United States did not disclose adult patients about their cancer diagnosis.¹⁵ However, in 1977, 97% (n = 256/264) had begun to provide more information on cancer diagnoses, which was a major change.¹⁶ The reasons for this may have been that the prognosis of patients had improved significantly because of advancements in cancer treatment, and that cancer had become more socially recognized.

TABLE 4. THE FREQUENCY TO DISCUSS FERTILITY ISSUES DIRECTLY TO CHILD AND ADOLESCENT PATIENTS

	<i>7–9 years</i>		<i>10–14 years</i>		<i>15–17 years</i>	
	<i>Japan</i>	<i>United States</i>	<i>Japan</i>	<i>United States</i>	<i>Japan</i>	<i>United States</i>
I do not tell anyone	8 (3.7%)	0 (0%)	4 (1.9%)	0 (0%)	2 (0.1%)	0 (0%)
Before cancer treatments start	17 (7.9%)	8 (40.0%)	88 (41.1%)	17 (85.0%)	162 (75.7%)	19 (95.0%)
I do not tell before cancer treatments, but discuss it after when they reach puberty or legal adults	43 (20.1%)	1 (5.0%)	46 (21.5%)	1 (5.0%)	12 (5.6%)	1 (5.0%)
I only tell the parents before cancer treatments start	138 (64.5%)	11 (55.0%)	54 (25.2%)	2 (10.0%)	16 (7.5%)	0 (0%)

TABLE 5. VARIABLES IDENTIFIED *A PRIORI* AS LIKELY TO BE RELATED TO TELLING A CHILD THEIR CANCER DIAGNOSIS

Cancer diagnosis		7–9 years		10–14 years		15–17 years	
		Japan	United States	Japan	United States	Japan	United States
MDS have a responsibility to tell children about their cancer diagnosis	Agree	149 (73.0%)	18 (90.0%)	190 (93.1%)	20 (100%)	199 (97.6%)	20 (100%)
Child's knowledge enhances participation in care decisions and improves compliance	Agree	161 (78.9%)	19 (95.0%)	193 (94.6%)	20 (100%)	196 (96.1%)	20 (100%)
Child's awareness dashes sense of hopefulness	Agree	12 (5.9%)	0 (0%)	13 (6.4%)	1 (5.0%)	14 (6.9%)	1 (5.0%)
Child should be told diagnosis only by parent	Agree	23 (11.3%)	0 (0%)	17 (8.3%)	0 (0%)	12 (5.9%)	0 (0%)
Fertility discussion							
MDS have a responsibility to tell children about the risk of gonadal dysfunction/future infertility	Agree	98 (48.0%)	11 (55.0%)	176 (86.3%)	18 (90.0%)	197 (96.6%)	20 (100%)
The parents should describe the risk of gonadal dysfunction and/or the risk of future infertility to the child	Agree	33 (16.2%)	8 (40.0%)	37 (18.1%)	7 (35.0%)	36 (17.7%)	7 (35.0%)
It is better to have teaching aids to explain the risk of gonadal dysfunction and/or the risk of future infertility	Agree	187 (91.7%)	14 (70.0%)	196 (96.1%)	14 (70.0%)	198 (97.1%)	13 (65.0%)

In Japan, historically, there has been a dominant paradigm in which the will of the family has been emphasized.^{17–19} In a 1991 study, 69.4% (344/494) of adult patients complained they wanted to know their cancer diagnosis, but only 31.8% of families wanted their own families to be notified of their cancer.²⁰ As the Japanese guidelines (Japanese National Cancer Center) published in 1998 recommend that cancer diagnosis disclosure be given directly to patients, the idea of “not telling” has shifted to the idea of “telling.”^{21–24}

Regarding cancer diagnosis disclosure to pediatric patients, it has generally been thought that pediatric patients should not know about a diagnosis of cancer, as in the case of adult patients.^{25,26} However, as the prognosis of such patients has improved because of advancements in cancer treatment, the notion of cancer diagnosis disclosure to pediatric patients has gradually changed.²⁷ Previously, only parents were informed; patients with childhood cancer were not informed of why they were being treated, which often resulted in anxiety.

However, if the patient knows about disease, then the patient can actively work on treatment, and parents can even intervene. We previously confirmed the merits of maintaining relationships of trust between patients and parents.²⁶ However, the proliferation of childhood cancer diagnosis disclosure has been slower in Japan than in the United States. In Japan, the Basic Plan to Promote Cancer Control Programs was revised in 2018,²⁸ and types of patient support such as job assistance and reductions in the cost burden of FP therapy were intensified.

Informed provision regarding the risk of gonadal dysfunction and future infertility

Our results showed a significant difference in the direct disclosure regarding the infertility risk to patients with childhood cancer between Japan (8%) and the United States (40%), especially between those aged 7–9 years, suggesting that the United States may be more actively providing information to children. The fact that the age of exposure to sex education in public schools in the United States is slightly younger than that in Japan is also one of the reasons why the U.S. physicians tell pediatric patients about sexual function, including FP treatment.^{29–32}

In addition, in the United States, there is an extensive FP program in which FP treatment options involving multiple co-medical staff can be proposed. Collaboration to drive the decision-making process for patient FP treatment among not only physicians and nurses, but also patient navigators, clinical psychologists, pharmacists, and social workers specializing in cancer reproductive medicine, is very important. The Oncofertility Consortium has developed a national network of institutions called the national physicians cooperative (NPC), which is dedicated to preserving the fertility of patients with cancer and other conditions whose progression or treatment may impair fertility.

Between 2007 and 2017, the NPC created a variety of materials such as educational materials and textbooks while working to provide more pediatric and adult patients with the

option of FP.³³ At least 144 FP programs currently exist according to a survey conducted in the United States.³⁴ FP programs can also be accessed directly by patients through a website or telephone. Overall, we assume that increased comfort of providers in the United States as well as the cultural acceptability of discussing future fertility of pediatric patients were the main reason that FP discussion occurs more often in the United States.

In contrast, in Japan, few hospitals have constructed a specific system, and in most cases, physicians play a central role in presenting patients with FP therapy options. According to a previous report, half of the 395 institutions that participated in a survey reported that FP options were explained by physicians and nurses, whereas 20% of the institutions reported that only physicians explained the FP options.³⁵ There is an urgent need to build a system for providing information on FP in Japan soon. In 2020, the JSFP began efforts to start a certification program for patient navigators, which are the core of the consultation system at each facility. Also, after the JSCO published the Clinical Practice Guidelines for Fertility Preservation in Pediatric, Adolescent, and Young Adults with Cancer, the concept of FP was addressed, with a survey finding that interest among medical professionals was increasing.^{35,36}

One limitation of this study was the small number of responders and the frequency of discussing fertility issues is overestimated. In the future, more participants are needed for further analysis. Another limitation is the gender ratio of the disseminated population is unknown there is a possibility that there is a difference between male and female, which may affect the answer.

Development of videos for FP therapy

The United States has many videos, such as “A New You, That’s Who”³⁷ and “Ovarian Tissue Cryopreservation” created by the Oncofertility Consortium, as well as videos developed by a children’s hospital. In contrast, in Japan, there is a video explaining FP treatment for adults, but no such video for children. Therefore, in this study, >90% of medical professionals perceived a need for educational materials, which led our research group to create three types of videos. For the prepubertal versions, it was necessary to consider the choice of simple language, the simplicity of the story, and the ability to alleviate the fear of cancer treatment and OTC.

For the pubertal version, we focused on including details of FP treatment for both females and males. Hopefully, these videos can increase the hope of such patients to be able to have their own child in the future by helping to overcome the barriers associated with discussing fertility issues with children. However, another limitation of this study is that we assessed the videos with only health care professionals; further prospective intervention trial in assessments with childhood and adolescent patients with cancer and their parents are needed, because parents have a great influence on their children’s decision-making.

Conclusions

The findings of the survey revealed that cancer diagnosis disclosure for pediatric patients is more widespread in both Japan and the United States compared with a decade ago. In contrast, there are fewer opportunities to discuss future infertility risk in Japan than in the United States. The resultant

materials are the first step in bringing concordance to communication patterns for emerging cancer care around the globe and that this study and its intervention arm provide guidance in ways that ensures global equity in care.

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Authors’ Contribution

Investigation, analysis, writing—original draft, and editing by Y.I. Project administration, data curation, and writing—review and editing by S.T. Resources, review, and editing by H.I., K.M., M.H., J.T., A.M., Y.C., T.I., T.M., M.M., D.K., T.K., T.M., and N.S. Investigation and writing—review by T.K.W. Conceptualization and writing—review and editing by N.S.

Author Disclosure Statement

The authors declare no conflicts of interest.

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Supplementary Material

Supplementary Data S1
Supplementary Data S2
Supplementary Data S3
Supplementary Data S4
Supplementary Data S5
Supplementary Data S6
Supplementary Data S7
Supplementary Data S8
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Supplementary Data S10

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Address correspondence to:

Nao Suzuki, MD, PhD
 Department of Obstetrics and Gynecology
 St. Marianna University School of Medicine
 2-16-1 Sugao, Miyamae-ku, Kawasaki
 Kanagawa 216-8511
 Japan

Email: nao@marianna-u.ac.jp