

Questionnaire surveys targeting Japanese pediatric endocrinologists regarding reproduction in pediatric and adolescent cancer patients

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Background

- With improvements in the treatment prognosis of cancer, the number of **childhood cancer survivors (CCSs)** has increased.
- Even though their **high incidence of gonadal dysfunction or subfertility** as late complications (late effects) has been recognized, a small number of surveys have been conducted in Japan.

Aim

- To assess physicians' opinions and reveal the current status of clinical practice in order to investigate issues associated with reproduction in Japanese pediatric or adolescent cancer.

Subjects and methods

• **178 directors or counselors of the Japanese Society for Pediatric Endocrinology (JSPE)** (male 139, female 39)

• First questionnaire survey was consisted of **36 questions** regarding the attributes of respondents, experiences with the follow-up, opinions on gonadal function or fertility, current status of clinical practice. **Free entry field** asking what would be necessary in the future to maintain gonadal function or preserve fertility.

• Approved by the Ethical Review Board of Osaka university hospital (No. 15203) .

• **Joint study** by the "working panel on compiling evidence regarding the fertility of long-term survivors who developed cancer during childhood or adolescence and developing a reproductive medicine network" (organizer: Yoko Miyoshi), which is a **research grant project for the promotion of cancer management** supported by the Japanese Ministry of Health, Labour and Welfare, and the "CCS Committee of JSPE".

Results: first questionnaire survey

Status of questionnaire responses

• **Response rate: 84.8% (151 valid responses)** Male: 82.7%: Female: 92.3%

• Majority of respondents were practicing in large-scale institutions.

• Existence in the same institution: Pediatric oncologists 62.9%
Reproductive specialists 53.6%

• Experience with clinical practice in CCS: 94.7%, Long-term follow-up: 74.8%

Current status of clinical practice

• More than half of endocrinologists examined patients **after cancer treatment** and, in most cases, who were experiencing physical issues.

• Providing explanations regarding treatment-related gonadal dysfunction before the treatment:

"Yes" 58.9%, "No" 2.0%, "Not sure" 25.8% , "By the oncologists" 88.8%

• Providing explanations on treatment-related subfertility:

"Yes" 54.3%, "No" 4.6%, "Not sure" 22.5% , "By the oncologists" 90.2%

• Experience with childbirth in CCS: 16.6% (n=25)

Opinions about maternal/ fetal problems in CCS

• Increase of miscarriages, premature births, delivery problems:
"strongly agree" or "agree" 66.9%

• Increase of fetal malformation: "strongly agree" or "agree" 27.8%

Actual experience with difficult situations due to subfertility or maternal health problems: 25.2% (n=38)

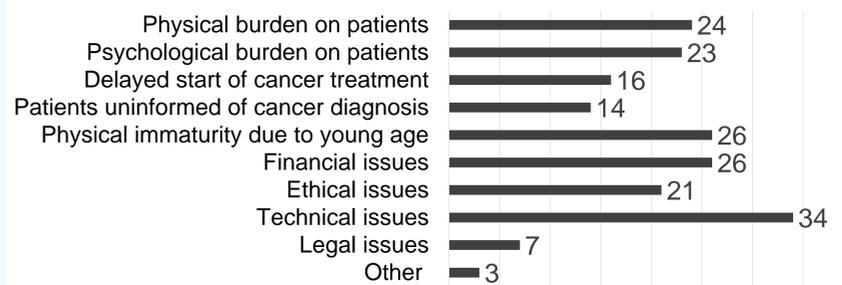
• Inadequate explanation before the treatment, shock of being informed by endocrinologists and not by oncologists, difficulty in the absolute evaluation of infertility, issues related to fertility itself, difficulty in selecting treatment for patients with recurrent cancer who desire to have children, disagreement between the opinion of patients and guardians, etc.

Issue with fertility preservation before the cancer treatment

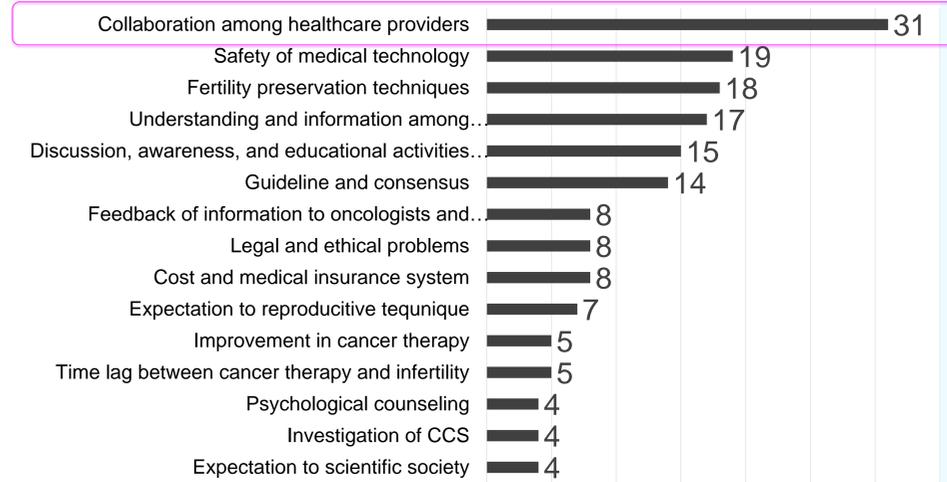
• Experience with fertility preservation: 15.2% (n=23)

• Existence of issues with fertility preservation:

"Yes" 22.5%, "No" 29.8% "Cannot decide" 45.7%



Necessities to maintain gonadal function and preserve fertility (n=71)



Results: second questionnaire survey

1. Status of questionnaire responses

• **35 answers from 39 subjects (response rate 100%)** who indicated experience with childbirth in CCSs or fertility preservation in the first survey.

• Some answers were received cooperatively from multiple respondents belonging to the same hospital.

2. Experience with Childbirth in CCSs (27 answers)

male CCSs: 16 answers

female CCSs: 22 answers

3. Health issues of pregnancy or childbirth in CCSs

a) Children born to male CCSs

No abnormalities (10), Unknown (6)

b) Children born to female CCSs

No abnormalities (14), Unknown(3)

Health issues of mother (1), child (3), mother and child(1)

Premature birth, low birth weight babies, delivery problem

No fetal malformation

4. Experience with fertility preservation (25 answers)

a) **Fertility preservation in males (21 answers)**

Sperm cryopreservation 16

Testicular tissue cryopreservation 2

Gonadal shielding before radiotherapy 10

b) **Fertility preservation in females (17 answers)**

Ovarian cryopreservation 3

Ovarian tissue cryopreservation 4

Gonadal shielding before radiotherapy 9

Ovarian transposition before radiotherapy 4

Gonad suppression with LHRH analog 7

5. Person who suggested fertility preservation

Medical care provider (21), Guardian (1), Patient (1), Unknown (1)

6. Details of childbirth and issues regarding fertility preservation (27 answers)

• Various difficulties and problems with fertility preservation

• Unexpectedly conception in 7 women under estrogen replacement therapy

• Gonadal function and fertility are important for childhood cancer survivors.

• We have to develop a unified guideline for management of their fertility.

• A nationwide survey on maternal health and childbirth of CCS is needed.

Conclusion

• Miyoshi Y, et al. Endocrinological analysis of 122 Japanese childhood cancer survivors in a single hospital. *Endocr J* 2008; 55: 1055-63.

• Miyoshi Y, et al. Low serum concentrations of anti-Müllerian hormone are common in 53 female childhood cancer survivors. *Horm Res Paediatr* 2013; 79: 17-21.

• Miyoshi Y, et al. Gonadal function, fertility, and reproductive medicine in childhood and adolescent cancer patients: a national survey of Japanese pediatric endocrinologists. *Clin Pediatr Endocrinol.* 2016;25:45-57.

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