

GYNECOLOGY

Reproductive outcomes of 105 malignant ovarian germ cell tumor survivors: a multicenter study



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BACKGROUND: Malignant ovarian germ cell tumors usually occur in young women. Until the 1970s, before establishment of systemic chemotherapy, malignant ovarian germ cell tumors had a very poor prognosis. Recently, prognosis has improved, and fertility-sparing treatment is being adopted in patients who desire to become pregnant. However, the number of malignant ovarian germ cell tumor survivors who actually became pregnant remains unknown.

OBJECTIVE: The present study aimed to clarify the reproductive outcomes in malignant ovarian germ cell tumor survivors by using data from a multicenter database and an additional survey on reproductive outcomes.

STUDY DESIGN: The study used the Tokai Ovarian Tumor Study Group database on ovarian cancer patients. We assessed the database from 1986 through 2016 and selected malignant ovarian germ cell tumor patients <40 years of age who received fertility-sparing treatment. Questionnaires on reproductive outcomes were sent to the registered facilities. The following data were collected and used in this study: age, date of onset, surgical procedure, chemotherapy regimen, tumor type, International Federation of Gynecology and Obstetrics stage, survival outcome and period, number of pregnancies and childbirths, marital

status, childbearing desire, method of pregnancy, gestational weeks at delivery, birthweight of the baby, obstetric complications, and menstrual status after fertility-sparing treatment.

RESULTS: A total of 110 malignant ovarian germ cell tumor patients who received fertility-sparing treatment were identified. The median follow-up period was 10.4 years. Five patients were excluded because of death or loss of fertility after treatment for recurrence. Thus, 105 patients were finally included. The additional survey revealed that 42 of 45 patients who desired childbirth became pregnant. The total number of pregnancies was 65, and 56 babies were born to 40 malignant ovarian germ cell tumor survivors.

CONCLUSION: The reproductive outcomes of malignant ovarian germ cell tumor survivor are promising with fertility-sparing treatment. Malignant ovarian germ cell tumor survivors can become pregnant and give birth if they desire.

Key words: bleomycin/etoposide/cisplatin therapy, cancer survivor, fertility-sparing treatment, malignant ovarian germ cell tumor, reproductive outcome

Introduction

Malignant ovarian germ cell tumors (MOGCTs) usually occur in young women,¹ and they account for 1–2% of all ovarian malignancies.² Until the 1970s, before establishment of systemic chemotherapy, MOGCTs had a very poor prognosis. However, after the introduction of chemotherapy consisting of bleomycin, etoposide, and cisplatin (BEP) for MOGCT treatment, the prognosis dramatically improved.³ Moreover, as BEP therapy has little effect on ovarian function, most MOGCT patients treated with BEP were

able to remain fertile and give birth.^{4–16} However, the number of MOGCT survivors who actually became pregnant remains unknown, as there is a relatively long period from MOGCT treatment to pregnancy because age at first marriage or childbirth is increasing, especially in Japan.¹⁷ The present study aimed to clarify the reproductive outcomes in MOGCT survivors by using data from a multicenter database and an additional survey on reproductive outcomes.

Materials and Methods

The Tokai Ovarian Tumor Study Group includes Nagoya University Hospital and 13 other institutions, and its database has been collecting ovarian cancer patient data since 1986, with approval from our ethics committee. All surgical specimens were pathologically reviewed by specialist gynecological pathologists blinded to the clinical data of patients. We screened the database from 1986 through 2016 and selected MOGCT

patients <40 years of age. We further identified patients who underwent fertility-sparing treatment (FST). In this study, FST was defined as preservation of the uterus and at least 1 ovary during surgery with any chemotherapy regimen but without adjuvant radiation therapy to the entire pelvis. To obtain additional data on MOGCT patients who underwent FST, questionnaires on reproductive outcomes were sent to the registered facilities in December 2016, and all completed questionnaires were collected. The following data were collected and used in this study: age, date of onset, surgical procedure, chemotherapy regimen, tumor type, International Federation of Gynecology and Obstetrics (FIGO) stage, survival outcome and period, number of pregnancies and childbirths, marital status, childbearing desire, method of pregnancy, gestational weeks at delivery, birthweight of the baby, obstetrical complications, and menstrual status after FST.

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AJOG at a Glance

Why was this study conducted?

To describe the reproductive outcomes of survivors of malignant ovarian germ cell tumor (MOGCT).

Key findings

Over 90% of survivors of MOGCT <40 years of age who received fertility-sparing treatment and desired pregnancy became pregnant and gave birth.

What does this add to what is known?

This study demonstrated favorable reproductive outcomes for survivors of MOGCT, including women with advanced stage diagnoses.

TABLE 1**Characteristics of patients who received fertility-sparing treatment (n = 110)**

Median age, y (range)	22.8 (5.0–39.0)
Median follow-up, y (range)	10.3 (1.3–30.3)
Pregnancy history before FST, n	
Nullipara	71
Multipara	14
Unknown	25
Histological type, n	
YST	31
IMT	42
DYS	37
FIGO stage, n	
I	79
II	10
III	20
IV	1
Residual tumors, n	
Yes	14
Adjuvant chemotherapy, n	
Yes	76
Recurrence, n	11
Death because of disease, n	4

DYS, dysgerminoma; FIGO, International Federation of Gynecology and Obstetrics; FST, fertility-sparing treatment; IMT, immature teratoma; YST, yolk sac tumor.

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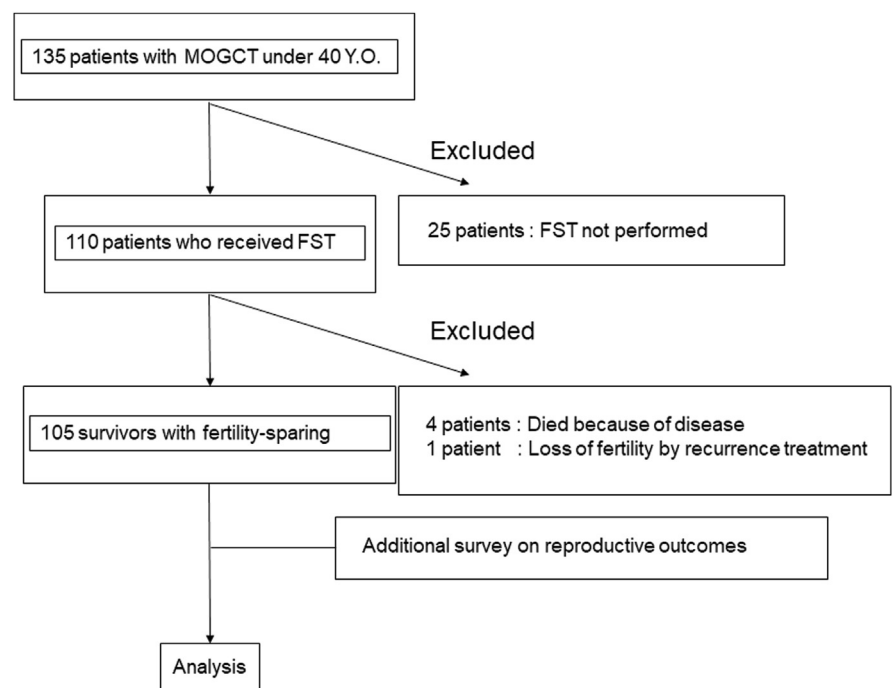
Results

Among 5057 patients with any ovarian cancer in the database, 135 patients with MOGCTs, who were aged <40 years, were selected. Of these patients, 25 were excluded because they did not receive FST. Thus, 110 patients who received FST were identified. Table 1 summarizes the patient characteristics. The median patient age was 22.8 years, and the median follow-up period was 10.3 years. Among the patients, 14 had a history of childbirth before FST. The tumor types

were as follows: 42 immature teratomas, 37 dysgerminomas, 31 yolk sac tumors. Recurrence was noted in 11 patients. One survivor of dysgerminoma recurrence received radiation therapy to the entire pelvis for the recurrence, and she lost fertility. Additionally, 4 patients died from MOGCTs. Thus, 105 MOGCT survivors who underwent FST were finally assessed (Figure 1).

The menstrual status after FST is summarized in Table 2. Regular menstruation recovered in 57 of 72 patients who received adjuvant chemotherapy. The median time to menstruation recovery was 6 months. At the time of the additional survey, 3 patients had premature ovarian failure at <40 years of age. The characteristics of these 3 patients are summarized in Table 3.

The obstetric outcomes after FST are summarized in Table 4. Among the 105 survivors, 45 attempted to become pregnant. Of these 45 patients, 42 achieved pregnancy, and 40 patients had successful deliveries. Seven patients received infertility treatment, but only 2 patients needed assisted reproductive technology.

FIGURE 1**Flowchart of patient inclusion**

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