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Is Omentectomy Mandatory Among Early Stage (I, II) Malignant Ovarian Germ Cell Tumor Patients? A Retrospective Study of 223 Cases

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Objective: The aim of the study was to investigate whether omentectomy (OMT) is necessary in the operation for apparently early stage malignant ovarian germ cell tumors (MOGCTs).

Methods and Materials: Searching medical records database of Sun Yat-sen University Cancer Center from January 1, 1966, to November 30, 2015, patients with MOGCTs were identified and their age, year of diagnosis, tumor grade, histologic subtype, International Federation of Gynecology and Obstetrics stage, nodal findings, gross observation of omentum, and performance of OMT were assessed. Overall survivals of patients with or without OMT were compared using Kaplan-Meier survival curves.

Results: A total of 223 MOGCT cases with clinically early stage (stage I and II) disease and with the 3 common histological subtypes of MOGCT were obtained, which include yolk sac tumor (YST), dysgerminoma (DSG), and immature teratoma (IMT). There were 192 stage I cases and 31 stage II cases. Fifty-four patients were diagnosed with YST, 61 with DSG, and 108 with IMT. Omentectomy was performed as part of the initial surgery in 74.0% patients (165/223) and was omitted in 26.0% patients (58/223). Chemotherapy was administered in 88.3% (197/223) of all patients. The median follow-up was 82.0 months. The 10-year overall survival rates of the patients with and without OMT were 90.5% and 98.1%, respectively ($P = 0.156$). Regarding different stages or histological subtypes, the 10-year survival rates of the 2 groups were 92.0% versus 97.9% ($P = 0.324$, stage I), 83.2% versus 100% ($P = 0.351$, stage II), 89.2% versus 100% ($P = 0.303$, YST), 94.1% versus 100% ($P = 0.470$, DSG), and 89.4% versus 96.0% ($P = 0.405$, IMT), respectively.

Conclusions: In conclusion, OMT in patients with clinically early stage MOGCT may not improve patient survival and may be omitted.

Key Words: Malignant ovarian germ cell tumor, Omentectomy, Clinically early stage

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Ovarian cancer is the most common cause of death from gynecologic malignancy. Malignant germ cell tumors (MOGCTs) account for approximately 15% of ovarian cancer and occur more frequently in teenage girls or young women. Immature teratoma (IMT), dysgerminoma (DSG), and yolk sac tumor (YST) are the 3 common types of MOGCT. Since

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1970s, the introduction of platinum-based chemotherapy into the treatment of MOGCT has dramatically increased the overall survival of patients. Now, the standard treatment of MOGCT is usually surgery followed by chemotherapy of BEP regimen (bleomycin, etoposide, and cisplatin). Currently, initial surgical style is mostly fertility-sparing surgery and comprehensive staging, which includes also omentectomy (OMT) in fertility-desired patients or comprehensive staging surgery in fertility not desired patients.

However, is OMT really necessary in early stage MOGCT? Recently, in clinically apparent early stage epithelial ovarian cancer, the significance of OMT was doubted. For epithelial ovarian cancer, extraovarian spread disease confined to the omentum is found in 2% to 7% of cases at most.[1] For patients without visible omental disease and for whom adjuvant chemotherapy is planned, OMT seems to be mainly for role of staging, although its therapeutic role remains unclear in microscopic omental disease.[1] As for MOGCT, few researches focused on this issue. One study recently suggested that staging surgery, in which OMT was included, for patients with apparently early stage MOGCT should be omitted.[2] Previously, our data in 45 patients with stage I or II YST showed that OMT might not improve patient survival.[3] In this study, we aim to further investigate the role of OMT on survival of patients with apparently early stage MOGCT.

MATERIALS AND METHODS

We retrospectively reviewed all cases with MOGCT treated at Sun Yat-sen University Cancer Center from January 1, 1966, to November 30, 2015. Approval for this study was granted by Sun Yat-sen University Cancer Center's Human Research Protection Office (YB2015-033-01). These cases were identified through hospital databases. Only patients diagnosed with IMT, DSG, and YST and with stage I to II disease were included. The patients' medical records were reviewed to collect case information including age, surgical procedures, operative findings, histopathology, International Federation of Gynecology and Obstetrics (2013) stage, adjuvant chemotherapy, and follow-up.

The software SPSS was used to analyze the data. We use the Kaplan-Meier method to calculate the survival rate. Overall survival was defined from the date of initial surgery to the time to death or last follow-up. When comparing the baseline of non-OMT (NOMT) and OMT groups, we used analysis of variance for age and cross-table method for the rest factors. A P value of less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

There are 457 patients who were diagnosed with the 3 types of MOGCT mentioned previously at our cancer center from January 1, 1966, to November 30, 2015. Among them, a total of 223 patients were diagnosed with early stage (stage I to II) disease, including 192 stage I cases and 31 stage II. The median (range) age was 25 (8–67) years. Fifty-four patients were diagnosed with YST, 61 with DSG, and 108 with IMT. Patient characteristics are listed in Table 1. Of all 223 patients, 165 (74.0%) received OMT as part of surgical procedures and 58 (26.0%) did not during the initial surgery. On the basis of OMT performed or not, we divided the patients into 2 groups. The following factors in the 2 groups were compared: age, stage, pathological subtype, other surgical procedure (hysterectomy or pelvic lymphadenectomy), and platinum-based chemotherapy. The mean age was 27.4 and 24.1 in patients with and without OMT, respectively. Of the group with OMT, 139 patients (84.2%) had stage I disease and 26 (15.8%) stage II; of the group without OMT, 53 patients (91.4%) had stage I disease and 5 (8.6%) stage II. As of tumor type, the number of patients with YST, DSG, or IMT were 43 (26.0%), 44 (26.7%), and 78 (47.3%), respectively, in the OMT group and that was 11 (19.0%), 17 (29.3%), and 30 (51.7%), respectively, in the group without OMT. Regarding adjuvant chemotherapy, 139 patients (84.2%) received platinum-based regimens in OMT group and 46 (79.3%) in the group without OMT. There was no significant difference in terms of age,

TABLE 1. Patient characteristics (N = 223)

Parameter	n (%)
Age, median (range), y	25 (8–67)
Stage	
I	192 (86.1)
I, NOS	25 (11.2)
IA	97 (43.5)
IB	4 (1.8)
IC	66 (29.6)
IC, NOS	9 (4.0)
IC1	30 (13.5)
IC2	24 (10.8)
IC3	3 (1.4)
II	31 (13.9)
II, NOS	11 (4.9)
IIA	2 (1.0)
IIB	18 (8.1)
Histopathology	
YST	54 (24.2)
Stage I	46 (20.6)
Stage II	8 (3.6)
DSG	61 (27.4)
Stage I	54 (24.2)
Stage II	7 (3.1)
IMT	108 (48.4)
Stage I	92 (41.3)
Stage II	16 (7.2)

NOS, not otherwise specified, we cannot clarify the specific stage from the data we got.

TABLE 2. Characteristics of the 2 groups: OMT done versus not done

Parameter	OMT Done (n = 165)	OMT Not Done (n = 58)	*P*
Mean age, y	27.4	24.2	0.085
Stage, (%)			
I	139 (72.4)	53 (27.6)	0.177
II	26 (83.9)	5 (16.1)	
Tumor type, (%)			
YST	43 (79.6)	11 (20.4)	0.278
DSG	44 (72.1)	17 (27.9)	0.698
IMT	78 (72.2)	30 (27.8)	0.560
Surgical procedure, (%)			
Hysterectomy	59 (35.8)	5 (8.6)	<0.001
Pelvic lymphadenectomy	79 (47.9)	3 (5.2)	<0.001
Lymph node biopsy	7 (4.2)	2 (3.5)	1.000
Platinum-based chemotherapy, (%)	139 (84.2)	46 (79.3)	0.390

stage distribution, tumor type, and the percentage of platinum-based chemotherapy between the 2 groups (all $P > 0.05$).

Patients who received OMT were more likely to have hysterectomy and pelvic lymphadenectomy (35.8% vs 8.6% and 47.9% vs 5.2%, respectively, both P values < 0.05) (Table 2).

Survival Analysis

The median follow-up time was 82.0 months. The 5- and 10-year overall survival rates for the 223 patients were 93.7% and 92.5%, respectively. Fourteen patients died and 209 survive up till now. The 5-year survival rates for patients with and without OMT were 92.2% and 98.1%, respectively ($P = 0.174$). The 10-year survival rates for the 2 groups were 90.5% and 98.1%, respectively ($P = 0.156$) (Table 3; Figs. 1A, B).

Among patients with stage I disease, 139 (72.4%) received OMT whereas 53 (27.6%) did not. The 5- and 10-year survival rates for patients with and without OMT were 94.1% versus 97.9% ($P = 0.366$) and 92.0% versus 97.9% ($P = 0.324$), respectively. Of the 31 stage II patients, 26 (83.9%) received OMT and 5 (16.1%) did not. The 5-year survival rates for patients with and without OMT were 83.2% and 100% ($P = 0.351$), respectively. The 10-year survival rates for the 2 groups were also 83.2% and 100% ($P = 0.351$), respectively (Figs. 1C, D).

Among 54 patients with YST, 43 (79.6%) received OMT and 11 (20.4%) did not. The 5-year survival rates for patients with and without OMT were 89.2% and 100%, respectively ($P = 0.303$), and the 10-year survival rates for the 2 groups were also 89.2% and 100%, respectively ($P = 0.303$). Likely, of 108 patients with IMT, 78 (72.2%) received OMT and 30 (27.8%) did not. The 5-year survival rates for patients with and without OMT were 89.4% and 96.0%, respectively ($P = 0.405$); the 10-year survival rates for the 2 groups were the same as the 5-year survival rate. As for the 61 DSG patients, 44 (72.1%) had OMT and 17 (27.9%) did not. None of them died in 5 years after initial surgery. Both groups' 5-year survival rate was 100%.

TABLE 3. Survival rate of patients with and without OMT as of different stages and histological subtypes

Group	5-y Survival Rate	*P*	10-y Survival Rate	*P*
Total	93.7	—	92.5	—
OMT	92.2	$P = 0.174$	90.5	$P = 0.156$
NOMT	98.1		98.1	
Stage I	95.1	—	93.7	—
OMT	94.1	$P = 0.366$	92.0	$P = 0.324$
NOMT	97.9		97.9	
Stage II	86.0	—	86.0	—
OMT	83.2	$P = 0.351$	83.2	$P = 0.351$
NOMT	100.0		100.0	
YST	91.4	—	91.4	—
OMT	89.2	$P = 0.303$	89.2	$P = 0.303$
NOMT	100.0		100.0	
DSG	100.0	—	96.0	—
OMT	100.0	None	94.1	$P = 0.470$
NOMT	100.0		100.0	
IMT	91.2	—	91.2	—
OMT	89.4	$P = 0.405$	89.4	$P = 0.405$
NOMT	96.0		96.0	

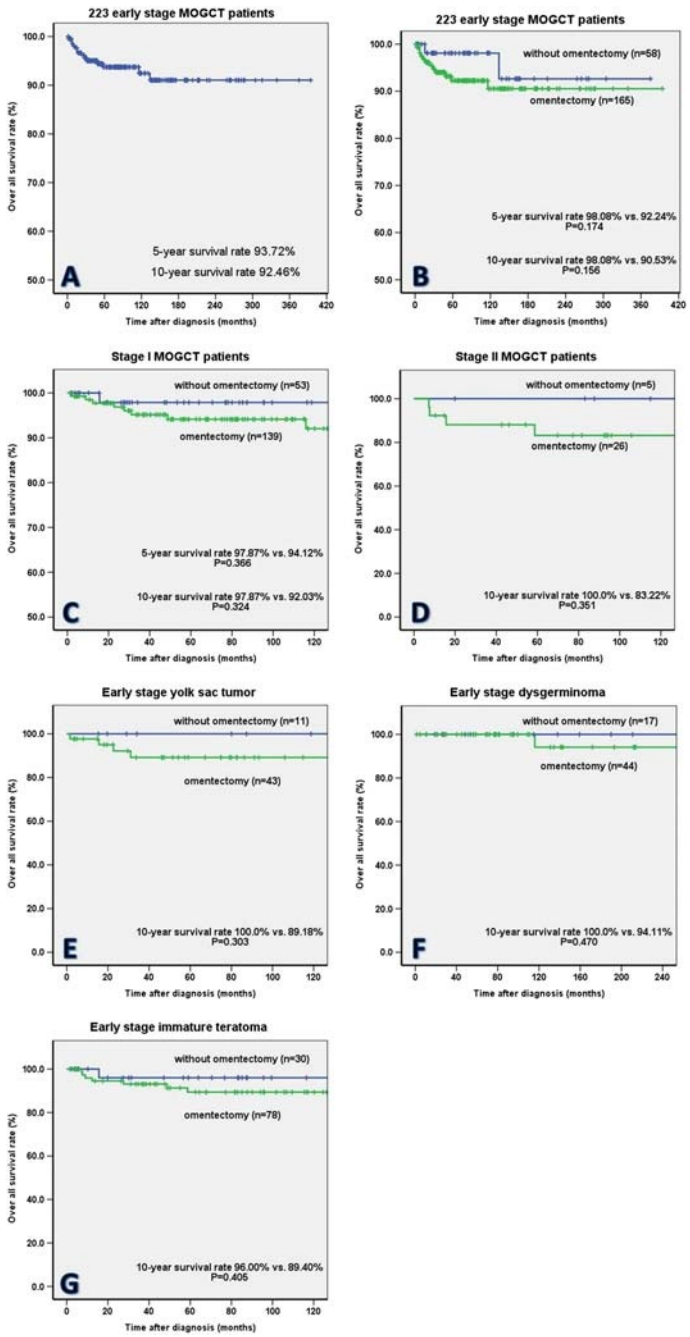

FIGURE 1. Survival rate of 223 patients with early stage MOGCT. A, The 5- and 10-year survival rates of the 223 patients with early stage MOGCT were 93.72% and 92.46%, respectively. B, A total of 165 patients in OMT group and 58 in NOMT group. The 5-year survival rates were 92.24% and 98.08%, respectively, for the 2 groups ($P = 0.174$). The 10-year survival rates were 90.53% and 98.08%, respectively ($P = 0.156$). C, There were 192 stage I patients, 139 (72.40%) of them received OMT while 53 (27.60%) did not. The 5-year survival rates were 94.12% and 97.87% ($P = 0.366$), respectively. The 10-year survival were 92.03% and 97.87% ($P = 0.324$), respectively. D. Of the 31 stage II patients, 26 were in OMT group and 5 in NOMT group. The 5- and 10-year survival rates were the same. The OMT group was 83.22% and the NOMT group was 100% ($P = 0.351$). E, The 54 YST patients had the same 5- and 10-year survival rate. They were 89.18% and 100% for OMT group (n = 43) and NOMT group (n = 11), respectively ($P = 0.303$). F, None of the 61 DSG patients died in 5 years after initial surgery. Both groups' 5-year survival rate was 100%. The 10-year survival rate of OMT group (n = 44) was 94.11% versus 100% for NOMT group (n = 17) ($P = 0.470$). G, In 108 IMT patients, the 5- and 10-year survival rates were the same. It was 89.40% for OMT group (n = 78) and 96.00% for NOMT group (n = 30) ($P = 0.405$).

TABLE 4. Multivariate analysis for 10-year overall survival

Parameter	*P*	RR	95% CI
Age (≥50 y vs <50 y)	0.005	7.262	1.824–28.908
Histopathology	0.913	1.038	0.531–2.029
Stage (I vs II)	0.559	1.457	0.413–5.148
OMT (yes vs no)	0.405	2.566	0.279–23.581
Hysterectomy (yes vs no)	0.398	1.920	0.422–8.727
Pelvic lymphadenectomy (yes vs no)	0.420	0.571	0.146–2.229
Platinum-based chemotherapy (yes vs no)	0.420	2.375	0.290–19.431

CI, confidence interval; RR, relative risk.

The 10-year survival rates for patients with and without OMT were 94.1% and 100%, respectively ($P = 0.470$) (Fig. 1E–G).

We perform a multivariate analysis using COX model to evaluate the impact of different factors on 10-year overall survival in terms of age, histology, stage, OMT, hysterectomy, pelvic lymphadenectomy, and platinum-based chemotherapy. The results revealed that only age is an independent prognostic factor for 10-year survival rate (Table 4), which also suggested that OMT may not be a prognostic factor.

DISCUSSION

Our study suggested that in patients with early stage MOGCT performing OMT may not improve patient survival. To our knowledge, this is one of the largest cohorts of patients thus far focusing on investigating the necessity of OMT in apparently early stage MOGCT.

Omentum is a peritoneal organ of different functions. It may play a role in protecting the peritoneal cavity and fighting infection.[4] Study showed that omentum may help heal injured or inflamed tissue or organ and prevent adhesion formation.[5] In the situation of cancer from peritoneal organ such as ovarian cancer, omentum may harvest the circulating cancer cells and prevent cell spread to greater extent.[5]

The therapeutic significance of OMT in ovarian cancer remains unclear. In epithelial ovarian cancer, OMT is traditionally recommended and included in the surgery for staging or as a part of tumor cytoreduction in early or advanced stage disease no matter whether there is macroscopic lesion. This is based on the considerations that ovarian cancer is easy to spread in the peritoneal cavity and omentum is the main metastasis site of tumor spread.[6] However, recently, the necessity of removing grossly normal omentum is doubted in early stage epithelial ovarian cancer.[5,7,8] Studies showed that the incidence of isolated metastasis to omentum is low (2%–7%) in patients with stage I and II epithelial ovarian cancer and with a macroscopically normal omentum. The rate is related to tumor stage, grade, and histology. Random biopsies instead of total OMT may be enough for staging purpose in clinically early epithelial ovarian cancer.[5] McNally et al[7] showed that OMT did not seem to improve patient survival in a retrospective series of 20,975 cases with stage I to IIIA epithelial ovarian cancer from the Surveillance, Epidemiology, and End Results Database.

In MOGCT, traditionally, complete staging surgery including OMT is also recommended as part of the surgical procedure in early stage disease (National Comprehensive Cancer Network guidlines).[6] However, few data in the literature are available supporting the rationality of OMT in this early situation. Thus, the prognostic significance of OMT in early stage MOGCT is uncertain. Studies showed that staging surgery, in which OMT is included as part of the procedure, in clinically early stage MOGCT may not improve patient survival compared with nonstaging patients.[2,9] In the study by Zhao et al,[2] 23 of 102 patients with clinically stage I MOGCT received staging surgery. The results showed that complete staging surgery was not a prognostic factor for disease-free survival.[2] Liu et al[10] analyzed the impact of staging surgery on survival in 92 patients with stage I to IV MOGCT, in which half received staging surgery and half nonstaging. Results showed that the tumor-free 5-year survival rates were 87% and 97% in the comprehensive staging surgery and nonstaging groups, respectively ($P = 0.115$).[10] In the literature, we did not find study that specially evaluated the usefulness of OMT on prognosis of patient with MOGCT. Our previous report on ovarian YST showed that OMT may not improve patient survival. Of the 66 patients, 45 had stage I and II disease; 36 of 45 patients received OMT during their initial surgery and 9 did not. The 5-year survival rates for patients with and without OMT were 89.2% and 100%, respectively ($P > 0.05$).[3] In this study, we also showed that the 5- and 10-year survival of patients with OMT is not higher than that of patients without OMT (92.4% vs 98.1%, 90.5% vs 98.1%). The results even favor the group without OMT. These results suggested that OMT in MOGCT may not help improve patient survival.

Why OMT did not confer survival improvement to patients with stage I and II MOGCT? First, these clinically early patients might have low incidence of microscopic metastasis to omentum as it is in epithelial ovarian cancer. Because our study did not include stage IIIA patients after pathological diagnosis, we cannot evaluate the occult metastasis rate of the omentum. In the literature, data addressing this issue are rare. In our previous report about ovarian YST, microscopic omental metastasis is found in only 2.7% patients (1/37) with grossly normal omentum.[3] In the report by Zhao et al[2] on 102 patients with MOGCT and with the disease grossly confined to the ovary, none of the 49 patients who received OMT had microscopic metastasis to the omentum.[2] Second, MOGCT is usually sensitive to chemotherapy, and postoperation chemotherapy is generally planned for MOGCT patients except those with stage IA DSG or IMT. For stage IA DSG or IMT, the frequency of microscopic metastasis to omentum is even lower because of the early disease, and surgical procedure without OMT in this situation is theoretically enough; for other clinically early stage diseases beyond the previous situation, the planned postoperation chemotherapy is possible to control the maybe microscopically metastasis on the omentum in the situation with the omentum left unremoved because the disease has high sensitivity to chemotherapy. Therefore, OMT might not have

therapeutic significance and might be omitted in patients with clinically early MOGCT.

Two other points should be considered. First, the group with OMT had more patients receiving hysterectomy and pelvic lymphadenectomy as compared with the group without OMT. Hysterectomy, OMT, and pelvic lymphadenectomy are traditionally included in the "staging" surgery of MOGCT. One main argue that more frequency of hysterectomy and pelvic lymphadenectomy in the OMT group may compromise the patient survival. To evaluate the prognostic impact of factors in terms of age, stage distribution, tumor type, chemotherapy, and surgical style on survival, we performed a multivariate analysis using COX model. The results showed that hysterectomy and pelvic lymphadenectomy are not independent prognostic factors. This is consistent to the report by Zhao et al,[2] which also suggested that complete staging surgery including hysterectomy and pelvic lymphadenectomy may not improve patient survival.

In conclusion, OMT in patients with clinically early stage MOGCT may not improve patient survival and may be omitted.

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