



Are omentectomy and lymphadenectomy necessary in patients with apparently early-stage malignant ovarian germ cell tumors?

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HIGHLIGHTS

- The role of omentectomy and lymphadenectomy is evaluated in clinically early-stage malignant ovarian germ cell tumors.
- Omentectomy and lymphadenectomy may be omitted in clinically early-stage malignant ovarian germ cell tumors.
- Omentectomy and lymphadenectomy do not improve survival in patients with clinically early-stage malignant ovarian germ cell tumors.

ABSTRACT

Objective To evaluate the role of omentectomy and lymphadenectomy in the treatment of clinically apparent early-stage malignant ovarian germ cell tumors.

Methods We retrospectively reviewed 245 patients with malignant ovarian germ cell tumors (yolk sac tumor, dysgerminoma, and immature teratoma) and with clinically early-stage disease, who were treated at Sun Yat-sen University Cancer Center between January 1, 1970 and December 31, 2017. The survival of patients who underwent either omentectomy or lymphadenectomy, or both (omentectomy/lymphadenectomy group) was compared with that of patients who did not undergo omentectomy or lymphadenectomy (non-omentectomy/lymphadenectomy group).

Results Sixty patients were diagnosed with yolk sac tumor, 74 with dysgerminoma, and 111 with immature teratoma. Of these 245 patients, 216 patients had stage I disease, 28 patients had stage II, and 1 patient had stage IIIA. There were 190 patients who underwent omentectomy and/or lymphadenectomy and 55 patients in the non-omentectomy/lymphadenectomy group, respectively. In the omentectomy/lymphadenectomy group, 112 patients underwent both omentectomy and lymphadenectomy, 71 underwent omentectomy only, and 7 underwent lymphadenectomy only. Two hundred and fourteen of 245 patients (87.3%) received post-operative chemotherapy. Median follow-up was 73 months (range 1–388). The 10-year overall survival rates in the omentectomy/lymphadenectomy group and non-omentectomy/lymphadenectomy groups were 96.8% and 100%, respectively ($p=0.340$). Multivariate analysis evaluating all potential prognostic factors showed that omentectomy and lymphadenectomy are not prognostic factors for survival.

Conclusions Omentectomy and lymphadenectomy do not appear to improve survival and may be omitted in patients with clinically apparent early-stage malignant ovarian germ cell tumors.

Malignant ovarian germ cell tumors originate from primitive germ cells of the ovary and account for approximately 15% of all ovarian malignancies with the highest incidence in adolescents and young women.¹ The most common types of malignant ovarian germ cell tumors are immature teratoma, dysgerminoma, and yolk sac (endodermal sinus) tumor. Patients are often diagnosed during the reproductive years and have high sensitivity to platinum-based chemotherapy. Unlike high-grade serous epithelial ovarian cancer, many patients with malignant ovarian germ cell tumors present at an early-stage and have excellent outcomes. Thus, conservative surgery followed by platinum-based chemotherapy is the standard of care in patients with malignant ovarian germ cell tumors, while radical surgery may be considered for infertile or older patients. As for stage I dysgerminoma and stage I G1 immature teratoma, surgery alone followed by observation is recommended. Adjuvant chemotherapy for patients with stage IA G2–G3 and IB–IC is still controversial, and observation or chemotherapy is considered feasible.^{2–4} Furthermore, after a relapse, most patients can be salvaged with surgery and chemotherapy or with chemotherapy alone given the high chemo-sensitivity of malignant ovarian germ cell tumors.^{5,6} According to the National Comprehensive Cancer Network clinical practice guidelines, comprehensive staging surgery is recommended for clinically apparent early-stage malignant ovarian germ cell tumors and includes peritoneal cytologic examination, peritoneal biopsies or removal of any suspicious lesion, hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic and para-aortic lymph node dissection.⁷ However, lymphadenectomy is no longer considered part of the standard staging procedure according to the European Society for Medical Oncology.⁸ Therefore, there is still no consensus about the role of lymphadenectomy, and the need for

Table 1 Patient characteristics (N=245)

Parameter	n (%)
Median age, (range), years	24 (5–61)
FIGO stage	
I	216 (88.2)
IA	40 (16.3)
IB	2 (0.8)
IC	82 (33.5)
Unavailable	92 (37.6)
II	28 (11.4)
IIA	1 (0.4)
IIB	13 (5.3)
Unavailable	14 (5.7)
IIIA	1 (0.4)
Histopathology	
YST	60 (24.5)
Stage I	53 (21.6)
Stage II	6 (2.4)
Stage III	1 (0.4)
DSG	74 (30.2)
Stage I	66 (26.9)
Stage II	8 (3.3)
IMT	111 (45.3)
Stage I	97 (39.6)
Stage II	14 (5.7)

DSG, dysgerminoma; FIGO, International Federation of Obstetrics and Gynecology; IMT, immature teratoma; YST, yolk sac tumor.

omentectomy is also debated.^{9–11} In this study, we aim to evaluate the roles of omentectomy and lymphadenectomy in patients with clinically apparent early-stage malignant ovarian germ cell tumors.

Statistical analysis was carried out using SPSS software (version 20.0). Frequency distributions were compared using χ^2 tests. The survival rate was calculated using the Kaplan-Meier method. Overall survival was calculated from the date of initial surgery to the date of death or last follow-up. A p value <0.05 was considered statistically significant. The data of this study have been uploaded onto the Research Data Deposit public platform (www.research-data.org.cn) (RDDA2018000789).

A total of 245 patients with clinically apparent early-stage disease were identified. One hundred and ninety patients (77.6 %) were included in the omentectomy/lymphadenectomy group and 55 (22.4%) in the non-omentectomy/lymphadenectomy group. In the omentectomy/lymphadenectomy group, 112 patients underwent both omentectomy and lymphadenectomy, 71 patients underwent omentectomy only, and 7 underwent lymphadenectomy only. Stage distribution after surgery was as follows: 216 cases with stage I disease (40 IA, 2 IB, 82 IC, and 92 unavailable), 28 with stage II (1 IIA, 13 IIB, and 14 unavailable); and 1 with stage IIIA. Among all patients, 60 were diagnosed with yolk sac tumor, 74 with dysgerminoma, and 111 with immature teratoma. Median age was 24 years (range 5–61). Table 1 shows patient characteristics.

No omentum metastasis was found in any of the 183 patients who underwent omentectomy. One of 119 (0.8%) patients who underwent lymph node dissection had lymph node metastasis. Bilateral salpingo-oophorectomy was performed in 48 patients (19.6%), unilateral salpingo-oophorectomy in 165 patients (67.3%), unilateral salpingo-oophorectomy and contralateral ovarian biopsy in 26 patients (10.6%), and unilateral ovarian cystectomy in six patients (2.4%). Age, stage, pathological sub-type, surgery type, surgical duration, blood loss, and platinum-based chemotherapy were noted and compared in the omentectomy/lymphadenectomy and non-omentectomy/lymphadenectomy groups (Table 2). The median age was 24.8 and 22.5 years (p=0.08) in the omentectomy/lymphadenectomy group and non-omentectomy/lymphadenectomy group, respectively. The number of patients with stage I, II, and IIIA disease were 167 (87.9%), 22 (11.6%), and 1 (0.5%), respectively, in the omentectomy/lymphadenectomy group, and 49 (89.1%), 6 (10.9%), and 0, respectively, in the non-omentectomy/lymphadenectomy group (p=0.85). Histopathologically, there were 48 (25.3%), 56 (29.5%), and 86 (45.3%) patients with yolk sac tumor, dysgerminoma and immature teratoma, respectively, in the omentectomy/lymphadenectomy group and 12 (21.8%), 18 (32.7%), and 25 (45.5%) in the non-omentectomy/lymphadenectomy group, respectively (p=0.84). Surgery was performed either via laparotomy or laparoscopy in both groups. One hundred and seventy-one patients underwent laparotomy in the omentectomy/lymphadenectomy group and 52 in the non-omentectomy/lymphadenectomy group (p=0.42). Fertility-sparing surgery was performed in 141 patients (74.2%) in the omentectomy/lymphadenectomy group and in 51 patients (92.7%) in the non-omentectomy/lymphadenectomy group (p=0.003). Median operative time was 160.2 min and 116.0 min (p<0.001) in the omentectomy/lymphadenectomy group and non-omentectomy/lymphadenectomy group, respectively. Median blood loss was 160.8 mL and 163.8 mL (p=0.97) in the two groups; respectively. Post-operative adjuvant chemotherapy was administered to 214 (87.3%) patients, 165 (86.8%) in the omentectomy/lymphadenectomy group, and 49 (89.1%) in the non-omentectomy/lymphadenectomy group, respectively. In the omentectomy/lymphadenectomy group, 157 patients (82.6%) underwent platinum-based chemotherapy regimens and eight received non-platinum-based chemotherapy, while 47 (85.5%) received chemotherapy with platinum-based regimens in the non-omentectomy/lymphadenectomy group and two received non-platinum-based chemotherapy.

Median follow-up duration was 73.0 months (range 1–388). The 5- and 10-year overall survival rates for all patients were 98.9% and 97.5%, respectively. The 5- and 10-year survival rates for patients in the omentectomy/lymphadenectomy group and the non-omentectomy/lymphadenectomy group were 96.8% and 100%, respectively (p=0.34) (Table 3). Among patients with stage I disease, 167 patients (77.3%) were in the omentectomy/lymphadenectomy group and 49 (22.7%) in the non-omentectomy/lymphadenectomy group; the 5- and 10 year survival rates for stage I patients in the omentectomy/lymphadenectomy group and the non-omentectomy/lymphadenectomy group were 98.4% versus 100% (p=0.43) and 96.2% versus 100% (p=0.33), respectively. Of the 28 stage II patients, 22 patients (78.6%) underwent omentectomy/lymphadenectomy and six patients (21.4%) did not; the 5- and 10-year survival rate in both groups was 100%.

Table 2 Characteristics of the two groups: OMT/LN versus non-OMT/LN

Parameter	OMT/LN group (n=190)	non-OMT/LN group (n=55)	P value
Median age (range), years	24.8 (9-61)	22.5 (5-40)	0.080
FIGO Stage, (%)			0.855
I	167 (87.9)	49 (89.1)	-
II	22 (11.6)	6 (10.9)	-
III A	1 (0.5)	0 (0.0)	-
Histopathology, (%)			0.837
YST	48 (25.3)	12 (21.8)	-
DSG	56 (29.5)	18 (32.7)	-
IMT	86 (45.3)	25 (45.5)	-
Surgical style, (%)			0.003
Hysterectomy	49 (25.8)	4 (7.3)	-
Fertility-sparing	141 (74.2)	51 (92.7)	-
Surgical route, (%)			0.424*
Laparotomy	171 (90.0)	52 (94.5)	-
Laparoscopy	19 (10.0)	3 (5.5)	-
Operation time (min)	160.2 (45-450, n=166)	116.0 (45-265 , n=25)	<0.001
Blood loss (ml)	160.8(10-3500, n=159)	163.8 (5-3000 , n=25)	0.971
Adjuvant chemotherapy, (%)			0.659
Platinum-based	165 (86.8)	49 (89.1)	1.000*
Without platinum	157 (82.6)	47 (85.5)	-
Without chemotherapy, (%)	8 (4.2)	2 (3.6)	-
Without chemotherapy, (%)	25 (13.2)	6 (10.9)	-

*Fisher exact test

DSG, dysgerminoma; FIGO, International Federation of Obstetrics and Gynecology; IMT, immature teratoma; LN, lymphadenectomy; OMT, omentectomy; YST, yolk sac tumor.

Table 3 Survival rate of patients in OMT/LN group and non-OMT/LN group of different stages and histological subtypes

Group	n	5-year Survival Rate (%)	P value	10-year Survival Rate (%)	P value
Total	245	98.9	-	97.5	-
OMT/LN	190	96.8	0.340	96.8	0.340
non-OMT/LN	55	100		100	
Stage					
Stage I	216	98.4	-	96.2	-
OMT/LN	167	98.4	0.434	96.2	0.331
non-OMT/LN	49	100		100	
Stage II	28	100	-	100	-
OMT/LN	22	100	-	100	-
non-OMT/LN	6	100		100	
Histology					
YST	60	94.5	-	94.5	-
OMT/LN	48	94.5	0.468	94.5	0.468
non-OMT/LN	12	100		100	
DSG	74	100	-	94.7	-
OMT/LN	56	100	-	94.7	0.544
non-OMT/LN	18	100		100	
IMT	111	100	-	100	-
OMT/LN	86	100	-	100	-
non-OMT/LN	25	100		100	

DSG, dysgerminoma; IMT, immature teratoma; LN, lymphadenectomy; OMT, omentectomy; YST, yolk sac tumor.

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Among 60 patients with yolk sac tumor, 48 patients (80%) underwent omentectomy/lymphadenectomy and 12 patients (20%) did not; the 5-year survival rates for patients in the two groups were 94.5% and 100%, respectively ($p=0.47$), the 10-year survival rates for the two groups were the same as the 5-year survival rate. Of the 74 patients with dysgerminoma, 56 patients (75.7%) underwent omentectomy/lymphadenectomy and 18 patients (24.3%) did not; no patient died in the 5 years after the initial surgery, but the 10-year survival rates for the two groups were 94.7% and 100.0%, respectively ($p=0.54$). Of the 111 patients with immature teratoma, 86 patients (77.5%) underwent omentectomy/lymphadenectomy and 25 patients (22.5%) did not; the 5- and 10-year survival rates for patients in the two groups were both 100.0%. After univariate and multivariate analyses, the results showed that none of the factors (age, histology, stage, surgical route, hysterectomy, removal of retroperitoneal lymph node, omentectomy, and platinum-based versus non-platinum-based chemotherapy) were prognostic for 10-year survival (Table 2), also suggesting that omentectomy and lymphadenectomy are not predictive of survival.

For the surgical treatment of malignant ovarian germ cell tumors, the recent, European Society for Medical Oncology guidelines recommend that omentectomy is included as an important part of surgical staging and that lymphadenectomy be omitted⁸; however, National Comprehensive Cancer Network guidelines recommend that both omentectomy and lymphadenectomy are included in the staging procedure in malignant ovarian germ cell tumors.⁷ The inconsistency between the two guidelines suggests that consensus has not been reached on the significance of omentectomy and lymphadenectomy, which still deserves evaluation.

In this study, most patients (87.3%) underwent postoperative chemotherapy. The 5-year survival rates for patients who did and did not undergo omentectomy/lymphadenectomy were 96.8% and 100%, respectively ($p=0.34$). Multivariate analysis also showed that omentectomy and lymphadenectomy are not prognostic for survival. The current study data are consistent with data reported previously.^{12 13} Zhao et al reported that 23 of 102 patients with malignant ovarian germ cell tumors and tumors confined to the ovary had comprehensive staging surgery.¹² Eighty-nine patients (87.3%) received adjuvant chemotherapy. Univariate analysis showed that complete staging surgery was not predictive of survival. Billmire et al also showed that comprehensive staging surgery may not be helpful for young patients with malignant ovarian germ cell tumors.¹³ They evaluated 131 girls with malignant ovarian germ cell tumors of all stages and found excellent survival rates following conservative surgical resection and platinum-based chemotherapy. The authors concluded that pelvic lymphadenectomy, random peritoneal biopsies, and omentectomy are not mandatory and have little effect on survival if visual inspection and palpation are normal.

Previous data showed that metastasis of grossly normal omentum is quite low (0–2.7%).^{12 14} In the study from Zhao et al regarding malignant ovarian germ cell tumors confined to the ovary, no metastasis was found in 49 patients who underwent omentectomy.¹² In our previous study on yolk sac tumor of all stages, metastasis was found in 1 of 37 (2.7%) omentums that appeared normal.¹⁴ In the current study, no metastasis was found in the omentums. The metastatic rate of lymph nodes in most patients with early-stage malignant ovarian germ cell tumors is also low,

although not in patients with dysgerminoma. In the study by Mahdi et al, the lymph node metastatic rates for immature teratoma and dysgerminoma were 1.4% (7/516) and 11.3% (40/354), respectively.⁹ In our previous study on yolk sac tumors, none of the 16 patients with early-stage disease (stage I=12, stage II=4) who underwent lymphadenectomy had lymph node metastasis.¹⁴ In the present study, the lymph node metastasis rate was 0.8% (1/119). The low metastasis rate in clinically apparent early-stage malignant ovarian germ cell tumors suggests that omentectomy and lymphadenectomy may have a limited role in identifying metastasis and may be omitted for diagnostic purposes after careful intra-operative inspection.

Owing to the high chemo-sensitivity of malignant ovarian germ cell tumors and the high success rate of salvage treatment for recurrence in patients with malignant ovarian germ cell tumors, observation after initial staging surgery may prevent short- and long-term complications caused by chemotherapy and may be feasible for low risk, stage I patients.⁵ Selecting patients who have a low risk of recurrence and may benefit from avoiding chemotherapy is a treatment challenge. The risk factors for recurrence in clinically apparent early-stage malignant ovarian germ cell tumors include mainly yolk sac tumor histology or yolk sac tumor component in mixed malignant ovarian germ cell tumors and incomplete peritoneal staging.⁵ In cases of recurrence, salvage treatment is usually successful.^{5 6 15} Thus, for patients who receive adjuvant chemotherapy, such as patients with yolk sac tumor disease, it is reasonable not to remove a clinically normal omentum and lymph nodes. For patients with non-yolk sac tumor disease and apparent stage I malignant ovarian germ cell tumors and the potential to avoid post-operative chemotherapy, the decision to remove the grossly normal omentum and normal appearing lymph nodes in staging procedure is complicated and needs careful consideration. Because the metastatic rate is low for normal omentum and lymph nodes based on the literature^{9 12 14} and our study, it may be an option to omit omentectomy and lymphadenectomy for clinically normal omentum and lymph nodes in patients with early disease.

In epithelial ovarian cancer, minimally invasive surgery is not associated with poor survival in women with stage I disease.¹⁶ In early-stage malignant ovarian germ cell tumors, there are few reports of minimally invasive surgery. In the study by Nasioudis et al of 298 patients with stage I malignant ovarian germ cell tumors, those in the minimally invasive surgery group were less likely to undergo lymph node dissection and omentectomy. Minimally invasive surgery was associated with reduced hospital length of stay and unplanned re-admission rates. There was no difference between overall survival of the minimally invasive surgery group and the laparotomy group.¹⁷ In the current study, 223 patients underwent abdominal surgery and 22 patients underwent laparoscopy. Univariate and multivariate analyses showed that minimally invasive surgery does not adversely affect 10-year survival. However, the number of laparoscopy patients is small, and further studies are warranted to show the safety of minimally invasive surgery in this setting.

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