

Systematic para-aortic and pelvic lymphadenectomy in ovarian cancer. A literature review

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Received:
May 21, 2017
Revised:
June 14, 2017
Accepted:
July 23, 2017

Abstract

Ovarian cancer represents one of the most frequent gynecological malignancies. The risk of developing this malignancy increases with age, especially after menopause. Surgery remains the only potentially curative treatment for early stage ovarian cancer, and it usually consists in salpingo-oophorectomy, omentectomy, peritoneal biopsies, and lymphadenectomy. Some studies revealed that systematic lymphadenectomy in early stage ovarian cancer leads to higher survival rates, while others showed the opposite. Identification of the sentinel ganglion using indocyanine-green, through open or laparoscopic approach, can decrease postoperative morbidity associated with systematic para-aortic lymphadenectomy. In advanced ovarian cancer, the goal is to obtain the absence of residual disease, which increases the overall survival. In this setting, there is an ongoing debate regarding the best method, various authors recommending either systematic para-aortic and pelvic lymphadenectomy, or just the resection of bulky masses. After reviewing the available evidence, we may conclude that in patients with ovarian cancer the goal should be complete resection of the malignant disease, including grossly invaded or micro-metastatic lymph nodes. Extensive lymphadenectomy contributes to a more precise staging, but more studies are needed to reveal the subgroup of patients who benefit most regarding overall and progression-free survival.

Keywords: ovarian cancer, systematic lymphadenectomy, surgery

Introduction

Ovarian cancer represents one of the most frequent gynecological malignancies. The risk of developing this type of cancer increases with age, especially after menopause. In current clinical practice, this neoplasia is often diagnosed in advanced stages⁽¹⁾. The widespread usage of laparoscopy and transvaginal ultrasound, decreased the tumor stage in which the diagnosis is usually made⁽¹⁾. The exfoliated tumor cells spread early outside the pelvis, especially in the right paracolic and subphrenic spaces, due to the negative pressure associated with respiratory movements⁽²⁾. Therefore, surgical staging should include peritoneal washing and cytological analysis, random peritoneal samples, or biopsies of all the suspicious areas⁽³⁾. The lymphatic drainage of the ovary is done through two main pathways: along the ovarian vessels in the para-aortic nodes and along the uterine vessels in the iliac lymphatic compartment⁽⁴⁾. Systematic lymphadenectomy of the pelvis and para-aortic areas were proposed during surgical debulking for advanced ovarian cancer to increase the R0 resection rate. However, two randomized control trials failed to show a survival benefit for systematic lymphadenectomy^(5,6). On the other hand, extensive surgery comes with an increased rate of postoperative complications⁽²⁾.

The objective of this review of the literature is to compare the benefits in term of oncological outco-

mes and postoperative morbidity of routine pelvic and para-aortic lymphadenectomy in patients with ovarian cancer.

Methods

We have screened the PubMed/Medline database for all the articles relevant to this topic, published in English language between January 2000 up to September 2017. The search strategy used was: ((((((ovar[Title/Abstract]) OR ovarian[Title/Abstract])) AND cancer[Title/Abstract]) AND (((lymphnode[Title/Abstract]) OR lymph node[Title/Abstract]) OR lymphadenectomy[Title/Abstract])))) AND systematic (Figure 1 and 2).

Results

The primary treatment for early stage ovarian cancer, I and II according to FIGO classification, remains surgical procedure with hysterectomy, salpingo-oophorectomy, omentectomy, peritoneal biopsies, and lymphadenectomy⁽⁷⁾, and additionally, appendectomy in case for mucinous tumors⁽⁸⁾. The reported metastasis rate in the pelvic lymph nodes is between 8% and 15%, while for the para-aortic lymph nodes is between 5% and 24%⁽⁹⁾. There is diverging evidence throughout the literature, some studies showing that systematic lymphadenectomy in early ovarian cancer is associated with a higher survival rate, while others proved the opposite⁽¹⁰⁾ (Table 1).

According to the European Society of Medical Oncology Clinical Practice Guidelines, 30% of the cases initially classified as initial stage ovarian cancer, were reclassified in advanced disease after histopathological analysis of the lymph nodes. In patients with limited pelvis malignancy, the para-aortic lymph nodes were positive in about 9% of the cases with sampling technique, and 22% in cases with systematic lymphadenectomy⁽⁸⁾.

The decision to perform systematic lymphadenectomy should take into account the histological type, the degree of differentiation, and the CA-125 level at the time of diagnosis⁽¹⁷⁾.

Identification of the sentinel lymph nodes with indocyanine-green was proposed, to avoid systematic para-aortic lymphadenectomy in early ovarian cancer⁽¹⁸⁾. Thus, biopsy or regional lymph node resection can be performed on the positivity or negativity of the sentinel ganglion to decrease postoperative morbidity associated with systematic lymphadenectomy⁽¹⁸⁾.

In the advanced ovarian cancer, the role of surgery is indisputable⁽¹⁹⁾, resection of all the macroscopic disease⁽²⁰⁾ being associated with increased overall survival⁽²¹⁾. To achieve this goal, surgery may include extensive organ dissections, such as intestinal resections, peritoneal stripping, diaphragm resection, splenectomy and a more radical lymphadenectomy⁽²²⁾. The systematic lymphadenectomy is associated with certain drawbacks, such as prolonged operative time, increased blood loss, difficult postoperative recovery, and increased risk of pulmonary thromboembolism⁽²³⁾. Nowadays, the laparoscopic approach was also proposed in high-volume centers⁽²⁴⁾.

There is confusing evidence about the role of para-aortic lymphadenectomy or just resection of bulky para-aortic masses in advanced ovarian cancer^(14,18). Although an optimal surgical debulking improves survival^(25,26), a systematic lymphadenectomy in advanced ovarian cancer does not seem to be beneficial⁽¹⁰⁾.

Table 1

Studies comparing systematic lymphadenectomy with no lymphadenectomy in patients with ovarian cancer

Study	Country	Stage of the disease (FIGO)	Number of patients (systematic pelvic + para-aortic vs. resection of bulky nodes)	Overall survival	Progression free survival	Morbidity
Eoh et al. ⁽¹¹⁾	Korea	IIIC, IV	96 vs. 62	Hazard ratio = 0.250 (P<0.001)	Hazard ratio = 0.0629 (P=0.048)	-
Rungruang et al. ⁽¹²⁾	USA	IIIC	689 vs. 1182	44.9 vs. 40.5 months (P=0.007)	16.8 vs. 15.1 months (P=0.01)	-
Iwase et al. ⁽¹³⁾	Japan	IIIB-C, IV	86 vs. 38	Hazard ratio = 1.1 (P=0.74)	-	-
Gmyrek et al. ⁽¹⁴⁾	Poland	I, II, III, IV	211 vs. 258	-	-	Intraoperative: 4.74% vs. 4.65% (P=0.6) Postoperative: 14.83% vs. 3.1% (P=0.002)
Dell'Anna et al. ⁽¹⁵⁾	Italy	IA-IV	158 vs. 150	5-year OS: 63.5% vs. 67.4% (P=0.81)	5-year PFS: 40.9% vs. 53.8% (P=0.29)	8.8% vs. 2% (P=0.008)
Chan et al. ⁽¹⁶⁾	USA	III, IV	4260 vs. 9658	5-year disease specific survival: Hazard ratio = 0.911 (P=0.001)	-	-
Panici et al. ⁽⁵⁾	Italy	IIIB-C, IV	216 vs. 211	5-year OS: 48.5% vs. 47% (P>0.05)	5-year PFS: 31.2% vs. 21.6% (P<0.05)	27.7% vs. 18.4% (P=0.014)
Maggioni et al. ⁽⁶⁾	Italy	I, II	138 vs. 130	5-year OS: 84.2% vs. 81.3% (P<0.05)	5-year PFS: 78.3% vs. 71.3% (P<0.05)	14.49% vs. 12.3% (P>0.05)

The neoadjuvant chemotherapy seems to be non-inferior to surgery⁽²⁷⁾, while adjuvant chemotherapy is associated with improved overall and progression-free survival⁽²⁸⁾. In stage III tumors, the primary debulking surgery is associated with increased overall survival, while for stage IV disease neoadjuvant chemotherapy has the same effect^(29,30). The subgroup of patients benefiting from neoadjuvant chemotherapy may be identified by a combination of serologic markers, such as CA-125 and imagery; laparoscopy may be a viable option⁽³¹⁾. The indocyanine-green fluorescence imaging aids in the discovery of peritoneal metastases in advanced ovarian cancer. However, it cannot discrimi-

nate between benign and malignant tissues following neoadjuvant chemotherapy^(31,32).

Conclusions

After reviewing the available evidence, we may conclude that in patients with ovarian cancer the goal should be complete resection of the malignant disease, including grossly invaded or micrometastatic lymph nodes. Extensive lymphadenectomy contributes to a more precise staging, but more studies are needed to reveal the subgroup of patients who benefit most regarding overall and progression-free survival. ■

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