UNIVERSITY OF CALIFORNIA,
IRVINE

# Do Bilateral Oophorectomy with Hysterectomy and Omentectomy Improve Epithelial Ovarian Cancer Survival Rate Compared with Bilateral Oophorectomy Only?

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

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by

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# DEDICATION

To my mother and father
for nursing me with love and encouraging me to go on every adventure.

To my family and friends
who never left my side.

To my lovely dogs
for keeping me company on those hard times.

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# ABSTRACT OF THE THESIS

Do Bilateral Oophorectomy with Hysterectomy and Omentectomy Improve Epithelial Ovarian Cancer Survival Rate Compared with Bilateral Oophorectomy Only?

By

Muzi Lu

Master of Science in Epidemiology

University of California, Irvine, 2018

Distinguished Professor Hoda Anton-Culver, Chair

Due to the large number of affected women and poor prognosis of epithelial ovarian cancer (EOC), improving the treatment methods for epithelial ovarian cancer patients becomes a research priority to increase survival length and post-surgical quality of life. In this study, we used data from the California Cancer Registry to examine if complete surgery with bilateral (salpingo-)oophorectomy, abdominal hysterectomy, and omentectomy improve survival rates for early and advanced stage epithelial ovarian cancer. We employed Kaplan-Meier survival analysis and found that for early stage epithelial ovarian cancer, neither hysterectomy nor omentectomy could improve epithelial ovarian cancer survival. Patients who received complete surgery did not have significantly higher five-year survival rate compared to patients who received bilateral (salpingo-) oophorectomy only. Considering the aggressiveness and the effectiveness, complete surgery was not the best approach for early stage EOC patients. For advanced stage EOC patients, bilateral (salpingo-) oophorectomy with hysterectomy revealed a higher but non-significant five-year survival rate compared to bilateral (salpingo-) oophorectomy only. Complete surgery group had a significantly higher five-year survival rate compared to bilateral (salpingo-) oophorectomy with omentectomy. Together these suggested that hysterectomy in addition to bilateral (salpingo-)

oophorectomy was essential for improving advanced stage EOC five-year survival. However, omentectomy did not show significant effect on EOC five-year survival. Complete surgery group had a five-year survival rate similar to that of the bilateral (salpingo-) oophorectomy with hysterectomy group. Again, considering the aggressiveness and the effectiveness, complete surgery was not the best approach for advanced stage EOC patients.

# CHAPTER 1

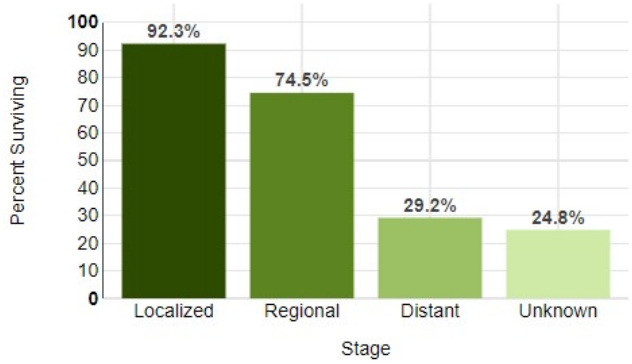
# INTRODUCTION

## Why study ovarian cancer?

According to U.S. Cancer Statistics data, cancer is the second leading cause of death in the United States[1]. Ovarian cancer is the fifth deadliest cancer among women in the United States, and it is the deadliest female gynecologic cancer[1]. Approximately 1.3% of women will develop ovarian cancer during their lifetime[2, 3]. SEER data suggests that there will be about 22,440 new ovarian cancer cases being diagnosed in the United States in 2018, and there will be an estimation of 14,070 deaths caused by ovarian cancer in 2018[2, 3].

To date, there is no effective screening for ovarian cancer[4]. Many patients do not have any symptom or only mild symptoms prior to being diagnosed with advanced stage ovarian cancer. Common ovarian cancer symptoms are bloating, pelvic or abdominal pain, trouble eating or feeling full quickly, and urinary symptoms[5]. Other symptoms like fatigue, back pain, and constipation are also seen in some patients[6]. However, these symptoms often overlap with other morbidities, not only ovarian cancer. Therefore, many patients ignore the early signs, or may not associate them with ovarian cancer. According to SEER statistics (2008-2014), about 59% of all ovarian cancer patients were diagnosed after cancer metastasis, and only about 15% of cases were diagnosed at early localized stage[2, 3].

**Figure 1.1 Ovarian Cancer 5-Year Relative Survival by Stage at Diagnosis**




*This figure is from the SEER website. It shows the age-adjusted rates of SEER 18 (2008-2014). Rates include all races and females only by SEER Summary Stage 2000*[2, 3].

Ovarian cancer survival rate is lower than other cancers among women. It is strongly related to the stage at diagnosis[2, 3]. The five-year survival rate for epithelial ovarian cancer (EOC) diagnosed at localized stage is about 92%, and that for regional stage is about 75%[2, 3]. However, the five-year survival rate for advanced/distant stage is very low, which is only about 29%[2, 3].

Ovarian cancer treatment depends on the stage at diagnosis. According to National Comprehensive Cancer Network guidelines, to achieve a better therapeutic effect, most of the early and advanced stage EOC patients should receive both chemotherapy and surgery[7]. For early stage IA-IB patients with less common histopathologies (non-serous EOC) or grade 1 endometrioid EOC surgical staging is required together with unilateral or bilateral oophorectomy. Other patients with stage IA-IV EOC should receive unilateral or bilateral oophorectomy with total abdominal hysterectomy, omentectomy and chemotherapy[7]. Debulking should also be considered if needed[7]. A previous study showed that adherence to National Comprehensive Cancer Network guideline for ovarian cancer treatment may help improve survival rate[8].

As the long-term survival after cancer diagnosis has improved over the years, surgical plan and post-surgical quality of life have become major issues in cancer treatment. The primary

reason for hysterectomy in EOC might be possible uterine metastasis and its impact on survival[9]. Menczer J et al. reported that out of 554 patients, 291 (52.5%) has uterine involvement. However, only 2.2% of stage II EOC patients had uterine involvement[9]. For serous type EOC, stage III and stage IV patients had statistically significantly higher uterine involvement compared to those with stage II tumors[9]. Since the aim of the surgery is to remove the primary tumor and achieve optimal cytoreduction, removing uterus in early stage EOC might be unnecessary, but in advanced stage it might improve long-term survival.

Similar to hysterectomy, the primary reason for omentectomy is to eliminate omental metastasis to improve survival. Nieman et al. found that ovarian cancer cells can spread through omentum and use the adipose tissue as fuel to increase the spreading speed[10], therefore, omentectomy may help improve ovarian cancer survival. However, another study by Yokoyoma et al. showed that omentum plays an important role in fighting cancer before it spread too much[11]. Omentum may also serve as a part of the immune barrier when exposed to tumor cells[12]. A recent study showed that omentectomy does not improve survival for early stage (<IIIA) ovarian cancer patients using SEER database[13] There is no study specifically focusing on the survival rate of advanced stage ovarian cancer patients with omentectomy.

Although hysterectomy or omentectomy alone might not improve early stage ovarian cancer survival, a study revealed that early stage ovarian cancer patients who performed complete surgery with abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy have higher long-term survival rate[14]. This suggests that there might be a combination effect of abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy on early stage ovarian cancer survival. No literature record regarding survival rate of advanced stage ovarian cancer patients with complete surgery was found.

In this study, we used data from the California Cancer Registry (CCR). Our main goal is to examine if complete surgery with bilateral (salpingo-) oophorectomy, abdominal hysterectomy, and omentectomy will improve early and advanced stage EOC five-year survival rate. We hypothesized that complete surgery would improve both early and advanced stage EOC five-year survival rate. We performed Kaplan-Meier survival analysis using adjusted models. All statistical analysis was done using SAS 9.4 software.

# CHAPTER 2

# BACKGROUND

## Ovarian cancer

### 2.1 Ovarian Cancer Biology

Ovary develops from the gonadal ridge[15]. It mainly consists of three types of cells: 1) germ cells which can proliferate and differentiate into oocytes, 2) epithelial cells which become the surface of the ovary, and 3) endocrine and interstitial cells which produce estrogen and progesterone[15]. All three types of cells can develop into benign or malignant tumor cells.

Even though the exact causes of epithelial ovarian cancer (EOC) are not clear, the "incessant ovulation" theory is the most commonly accepted[16]. This theory states that the surface epithelium of the ovary may suffer from ovulatory trauma and become predisposed to malignant tumors[16]. Another theory suggests that chemical carcinogens can enter the uterus and the fallopian tubes through the vulva and vagina which can cause inflammation and eventually become ovarian cancer[16].

**Table 2.1 Ovarian Cancer Types**

| |
|---|
| Surface Epithelium (About 90%) |
| Serous |
| Mucinous |
| Endometrioid |
| Clear Cell |
| Transitional Cell |
| Sex Cord-Strom (About 7%) |
| Granulosa Cell |
| Thecoma |
| Fibroma |
| Sertoli-Leydig |
| Steroid |
| Germ Cells (About 3%) |
| Dysgerminoma |
| Yolk Sac |
| Embryonal Carcinoma |
| Choriocarcinoma |
| Teratoma |

*Different ovarian tumors originate from different cell subtypes. Prevalence of malignant components in parentheses. [Reproduced from Chen VW et al.: Pathology and classification of ovarian tumors. Cancer. 2003. 97:2631[17].]*

About 90% of all malignant ovarian tumors are surface EOC[17]. EOC can be further divided into five subtypes: serous, endometrioid, mucinous, clear cell, and translational cell (very rare) tumors[17]. Sex-cord-stromal ovarian cancer accounts for about 7% of all ovarian cancer cases[17]. It arises from the connective tissue in the ovaries and can affect women in all ages[15]. Germ cell ovarian cancer usually affects younger women, and it accounts for about 3% of all ovarian cancer cases[17, 18]. In this study, we focused on EOC only.

About 52% of all EOC cases are serous carcinomas[19]. A three-tire grading system graded serous EOC from low to high as well differentiated, moderately differentiated, and poorly differentiated[18]. Grade 1, well differentiated, serous EOC usually has well-formed glands and papillary fronds[18]. Grade 2, moderately differentiated, serous EOC may have sheets of tumor cells with papillae[18]. Grade 3, poorly differentiated serous EOC mainly consists of sheets of

malignant cells[18]. A new two-tier grading system divides ovarian serous carcinomas into low- and high-grade[20-22]. The vast majority of ovarian cancer cases are high-grade serous EOC[23]. It consists of both cystic and solid components[18]. A recent study found that high-grade serous EOC originated in the fallopian tube, instead of ovaries[24]. Therefore, the malignant cells can spread into the abdominal cavity very early. By the time the tumor becomes symptomatic it is usually in the advanced stage.

EOC mainly spread through peritoneal dissemination and lymphatic dissemination[16]. With peritoneal dissemination, the tumor penetrates the ovarian capsule firs; then the malignant cells can enter the peritoneal cavity and implantation may occur on any abdominopelvic organs[16]. Common implantation occurs on the uterus, adnexa, omentum, bowel, and liver[16]. The malignant cells can also circulate around the body through lymph system[16]. Studies show that about 80% of ovarian cancer patients have lymph node metastases[25, 26]. Direct extension of the tumor can also occur[16]. As the tumor grows larger, the malignant cells can attach to the surrounding structures[18]. Hematogenous spread will occur when the malignant cells enter the blood vessels and circulate through the body; distant metastasis may occur in this case[16].

## 2.2 Epithelial Ovarian Cancer Stages

California Cancer Registry uses SEER Summary Stage program to classify tumor stage. Table 2.2 shows the specific SEER Summary Staging schema.

## Table 2.2 SEER Summary Staging Manual 2000- Ovary

**SUMMARY STAGE**

**0 In situ:**
- Noninvasive; intraepithelial
- Preinvasive

**1 Localized only**
- Tumor limited to one ovary, capsule intact, no tumor on ovarian surface
  FIGO Stage IA
- Tumor limited to both ovaries, capsule(s) intact, no tumor on ovarian surface
  FIGO Stage IB
- Tumor limited to ovary(ies):
  - Unknown if capsule(s) ruptured or if one or both ovaries involved
- Localized, NOS
  FIGO Stage I, not further specified

**2 Regional by direct extension only**
- Implants on ovary(ies)###***
- Tumor limited to ovary(ies), capsule(s) ruptured#*
- Tumor limited to ovary(ies) WITH malignant cells in ascites or peritoneal washingsa
- Tumor on ovarian surface###***
  FIGO Stage IC
- Extension to or implants###*** on:
  - Adnexab
  - Fallopian tube(s)b
  - Uterus***
    FIGO Stage IIA

**2 Regional by direct extension only (continued)**
- Extension to or implants on:
  - Pelvic tissue:
    - Adjacent peritoneum
    - Ligament(s):
      - Broadb
      - Ovarian
      - Round
      - Suspensory
    - Mesovariumb
  - Pelvic wall

  FIGO Stage IIB
- Extension to pelvic tissues or pelvic wall WITH malignant cells in ascites or peritoneal washingsa
  FIGO Stage IIC
- Extension*** or discontinuous metastasis*** to:
  - Bladder
  - Bladder serosa
  - Cul de sac (rectouterine pouch)
  - Parametrium
  - Rectosigmoid
  - Rectum
  - Sigmoid colon
  - Sigmoid mesentery
  - Ureter (pelvic portion)
  - Uterine serosa

  FIGO Stage II, not further specified

**3 Regional lymph node(s) involved only**
- REGIONAL Lymph Nodes (including contralateral or bilateral nodes)
- Aortic, NOS:###
  - Lateral (lumbar)
  - Para-aortic
  - Periaortic
- Iliac, NOS:
  - Common
  - External
  - Internal (hypogastric), NOS:
    - Obturator
- Inguinal***
- Lateral sacral (laterosacral)***
- Pelvic, NOS
- Retroperitoneal, NOS###
- Regional lymph node(s), NOS

**4 Regional by BOTH direct extension AND regional lymph node(s) involved**
- Codes (2) + (3)

**5 Regional, NOS**

**7 Distant site(s)/lymph node(s) involved**
- Microscopic peritoneal implants beyond pelvis, including peritoneal surface of liver
  FIGO Stage IIIA
- Macroscopic peritoneal implants beyond pelvis, <2 cm in diameter, including peritoneal surface of liver
  FIGO Stage IIIB

**7 Distant site(s)/lymph node(s) involved (continued)**
- Peritoneal implants beyond pelvis, >2 cm in diameter, including peritoneal surface of liver
  FIGO Stage IIIC
- Peritoneal implants, NOS
  FIGO Stage III, not further specified
- Distant lymph node(s)
- Further contiguous extension or metastasis:
  - Abdominal mesentery
  - Colon except sigmoid
  - Diaphragm
  - Gallbladder
  - Kidney
  - Liver (peritoneal surface)
  - Omentum
  - Pancreas
  - Pericolic gutter
  - Peritoneum, NOS (excluding adjacent pelvic peritoneum)
  - Small intestine
  - Spleen
  - Stomach
  - Ureter (retroperitoneal portion)
- Metastasis, including:
  - Liver parenchymal metastasis
  - Pleural fluid (positive cytology)

  FIGO Stage IV

**9 Unknown if extension or metastasis**

**Note 1:** Ascites, NOS is considered negative.

**Note 2:** Peritoneal implants outside the pelvis must be microscopically confirmed. Peritoneal implants may also be called seeding, salting, talcum powder appearance, or studding.

**Note 3:** If implants are mentioned, determine whether they are in the pelvis or in the abdomen and code appropriately to regional by direct extension or to distant. If not stated, code to distant.

a Since "cancer cells in ascites or in peritoneal washings" was not specifically categorized in either the Historic Stage or in the 1977 Summary Staging Guide, previous cases may have been coded to either regional or distant.

b Involvement of contralateral fallopian tube, broad ligament, mesovarium, or adnexa was considered distant in 1977 Summary Staging Guide.

# Considered localized in Historic Stage
### Considered distant in Historic Stage
* Considered localized in 1977 Summary Staging Guide
*** Considered distant in 1977 Summary Staging Guide

*Reprinted from: Young JL Jr, et al., SEER Summary Staging Manual - 2000: Codes and Coding Instructions. National Cancer Institute, NIH Pub. 2001. No. 01-4969, Bethesda, MD*[38].

## 2.3 Epithelial Ovarian Cancer Treatments

Ovarian cancer treatment plan largely depends on the stage at diagnosis. According to National Comprehensive Cancer Network guidelines, to achieve a better therapeutic effect, most of the early and advanced stage EOC patients should receive both chemotherapy and surgery[7]. For early stage IA-IB patients with less common histopathologies (non-serous EOC) or grade 1 endometrioid EOC surgical staging is required together with unilateral or bilateral oophorectomy[7]. Chemotherapy is not required[18]. Other patients with stage IA-IV EOC should receive unilateral or bilateral oophorectomy with total abdominal hysterectomy, omentectomy, and chemotherapy[7]. Debulking should also be considered if needed[7].

Oophorectomy is the procedure that removes one (unilateral) or both side (bilateral) of the ovaries. If the patient is young, and fertility is still desired, unilateral oophorectomy may be performed to remove the affected ovary. Oophorectomy can be performed in conjunction with salpingectomy, the procedure which removes fallopian tube. Together the procedures are called salpingo-oophorectomy. Premenopausal women undergo bilateral oophorectomy will have a sudden drop in estrogen and progesterone levels, which leads to surgical menopause. Due to a sudden plunge in hormone levels, patients undergo surgical menopause usually experience intense menopausal symptoms than women with natural menopause[27, 28]. They may also have a higher risk of osteoporosis and cardiac disease[29-31]. As a surgery, oophorectomy may have a potential risk of organ injury (bowel, bladder, and ureter), vascular injury, nerve injury, and infections[32].

Hysterectomy is the procedure that removes the uterus. There are three types of hysterectomy. Supracervical hysterectomy removes the uterus but not the cervix. Total hysterectomy removes the entire uterus and the cervix. This is commonly performed on ovarian

cancer patients. In some rare cases, radical hysterectomy is performed which involves the removal of the uterus, tissues around the uterus, the cervix, and the upper vagina. Hysterectomy is considered major surgery. Patients may have a greater risk of hemorrhage, organ injury, fistula formation, and infections[33].

Omentum is a thin fold of tissue that covers the abdominal organs. Omentectomy is a procedure designed to remove the omentum. Omentectomy is recommended for patients with peritoneum metastasis or at high risk of peritoneum metastasis. There are two types of omentectomy. Supracolic omentectomy removes all omentum, while partial omentectomy removes the affected portion only. Patients with omentectomy may have increased risk of colon or mesocolon injury and infections[34]. Some recent studies showed that omentectomy might not be necessary for ovarian cancer patients as there was no obvious benefit found compared to the patients who did not perform omentectomy[11, 35].

# CHAPTER 3

# SPECIFIC AIMS AND METHODS

## 3.1 Overall Objectives

Due to the large number of affected women and poor prognosis of epithelial ovarian cancer (EOC), improving the treatment methods for epithelial ovarian cancer patients becomes a research priority to increase survival length and post-surgical quality of life. Our primary goal is to examine if complete surgery with bilateral salpingo-oophorectomy, abdominal hysterectomy, and omentectomy will improve early and advanced stage epithelial ovarian cancer (EOC) five-year survival rate using data from the California Cancer Registry (CCR).

Based on data from the CCR, we examined the patients with four different surgery groups:

1. Bilateral (salpingo-) oophorectomy only
2. Bilateral (salpingo-)oophorectomy with hysterectomy
3. Bilateral (salpingo-) oophorectomy with omentectomy
4. Complete surgery: Bilateral (salpingo-) oophorectomy with omentectomy and hysterectomy

## 3.2 Specific Aims:

A. To examine the five-year survival rates of early and advanced stage EOC patients with complete surgery (bilateral salpingo-oophorectomy, abdominal hysterectomy, and omentectomy).

   • We hypothesized that complete surgery (group 4) would have higher early and advanced stage EOC five-year survival rates compared with all the other surgery groups.

B. To examine the five-year survival rates of early and advanced stage EOC patients with hysterectomy.

• We hypothesized that hysterectomy would not improve early stage EOC five-year survival rate, but would improve advanced stage EOV five-year survival rate. Which means, for advanced stage patients, group 2 would have a higher five-year survival rate than group 1, and group 4 would have a higher five-year survival rate than group 3.

C. To examine the survival rates of early and advanced stage EOC patients with Omentectomy.

• We hypothesized that omentectomy would not improve early stage EOC five-year survival rate, but would improve advanced stage EOC five-year survival rate. For advanced stage, group 3 patients might have a higher five-year survival rate than group 1 patients, and group 4 patients might have a higher five-year survival rate than group 2 patients.

### 3.3 Study Design

This is a case-only study using data from the CCR. According to the Health and Safety Code, Section 103885, all new cancer cases diagnosed in California since January 1988 should be reported to the CCR. Approximately 99% of all ovarian cancer cases diagnosed in the state of California are reported to the CCR since that time[36]. Epithelial ovarian cancer patients diagnosed between January 1st, 1988 and December 31st, 2008 were included in this case-only study.

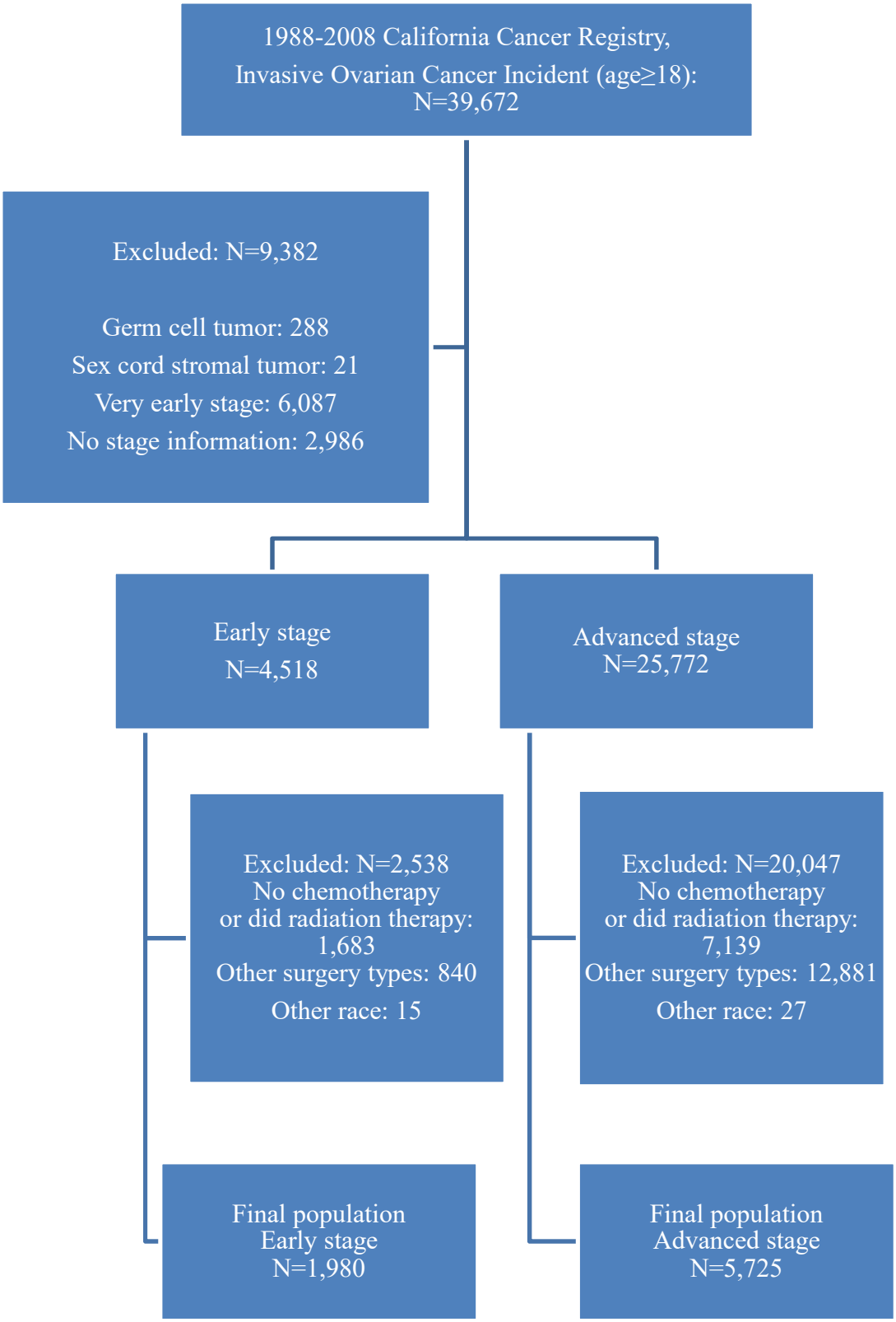
### 3.4 Study Population

As required by the law, an estimation of more than 99% epithelial ovarian cancer cases diagnosed in the state of California is reported to the CCR[36]. Patients diagnosed between January 1st, 1988 and December 31st, 2008 were included in this case-only study. Ovarian cancer cases

were identified from the CCR data using Surveillance, Epidemiology, and End Results (SEER) primary site recode 27040 and ICD-0-3 C569. Tumor behavior was classified in the CCR as benign, uncertain/borderline, in situ, and malignant/invasive. Only malignant/invasive cases were included in this study. There were 39,672 patients who were 18 years or older at diagnosis with first or only invasive epithelial ovarian cancer. Tumor stage was determined using a derived variable SUMSTAGE. The tumor stage is classified as in situ, localized, regional by direct extension, regional by lymph nodes, regional by direct extension and lymph nodes, regional NOS, remote, not abstracted, and unknown or not specified. We excluded the patients with no valid or detailed tumor stage information (N= 2,986). We also eliminated 6,087 patients who were at a very early stage (in situ and localized) and did not require hysterectomy or omentectomy. Regional by direct extension, regional by lymph nodes, and regional by direct extension and lymph nodes were defined as early stage. Remote was defined as advanced stage. Then, we limited the treatment types according to NCCN guideline. We excluded the patients who did not receive chemotherapy. Since radiation is not recommended for all patients, we also eliminated the patients with radiation therapy in both early stage group and advanced stage group, resulting in 2,835 patients in the early stage group (regional) and 18,633 patients in the advanced stage group (remote). We further limited the surgery type to the following four groups according to the CCR categories: Bilateral-oophorectomy without hysterectomy, Bilateral-oophorectomy with hysterectomy, Oophorectomy with omentectomy but not hysterectomy, and Oophorectomy with omentectomy and hysterectomy. Race/ethnicity was categorized according to the CCR data as non-Hispanic white (Caucasian), non-Hispanic black (African American), Hispanic, Asian/Pacific Islanders (Asian), American Indian, and Other/unknown. Due to the small sample size, the race/ethnicity was limited to non-Hispanic white, non-Hispanic black, Hispanic, and

Asian/Pacific Islander in this study. Social economic status (SES) in the CCR is defined by two derived variables QUINYOST (from year 1988 to 2005) and QUINYANGIMPUTED (from year 2005 to 2008). They stratify the SES to five categories: lowest, lower-middle, middle, higher-middle, and highest SES based on quintiles of the YOSTSCL score. YOSTSCL is an SES measurement based on the principal components analysis of census variables. The final population includes 1,980 patients in the early stage group and 5,725 patients in the advanced stage group.

**Figure 3.1 Population Selection**



## 3.5 Statistical Analysis

Patient demographical characteristics and clinical characteristics were analyzed using Pearson chi-square descriptive statistics. The primary goal of this study is to examine the five-year survival rate for each surgical treatment type. The survival time was calculated in months by counting the interval between the date of diagnosis and the date of death from any cause or loss to follow-up. The survival time was examined by Kaplan-Meier survival analysis. Multinomial logistic regression was employed to test which factors were significantly associated with survival. Cox proportional hazard regression model was used to investigate the independent effect of all predictor variable. All statistical analysis was performed using SAS 9.4 software.

# CHAPTER 4

# RESULTS

## 4.1 Early Stage Epithelial Ovarian Cancer

1,980 early stage epithelial ovarian cancer (EOC) patients diagnosed between 1988 and 2008 were included in this study (Table 4.1). The median age at diagnosis was 55 years old (range 18–88 years old) with a mean of 55.6 years old (±12.8 years old). 65.5% (1,296) subjects were non-Hispanic white females. 1,712 (86.5%) patients were in regional stage with direct extension only. Most patients with known tumor size had a tumor larger than 10cm (751, 37.9%). 33.8% (669) patients had a grade III tumor which was poorly differentiated.

Overall, 115 (5.8%) early stage EOC patients received bilateral (salpingo-) oophorectomy as the only surgery (Group 1), 504 (25.5%) patients received bilateral (salpingo-) oophorectomy with hysterectomy (Group 2), 201 (10.2%) received bilateral (salpingo-) oophorectomy with omentectomy (Group 3), and 1,160 (58.6%) received complete surgery: bilateral (salpingo-) oophorectomy with omentectomy and hysterectomy (Group4).

According to Pearson chi-square result, only age at diagnosis and race were statistically significantly ($p<0.05$) associated with surgery type selection. Patients who were diagnosed before 45 years old were more likely to be Group 3 (54, 26.9%). Patients who were diagnosed at 70 years or older were more likely to be Group 1 (39, 33.9%). Unlike Asian/Pacific Islander who were more likely to be Group 4 (184, 15.9%), few non-Hispanic black patients were in this group (28, 2.4%).

As shown in Table 4.2, we noticed that race/ethnicity was statistically significantly associated with socioeconomic status (SES, $p<0.05$). Non-Hispanic white patients were more

likely to have highest SES (401, 78.3%), while non-Hispanic black and Hispanic patients were more likely to have the lowest SES (21, 8.0%; 119, 45.4%).

**Table 4.1 Early Stage Epithelial Ovarian Cancer Patient Characteristics**

| Characteristics | All | | Group 1 Bilateral Oophorectomy | | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | | Group 4 Bilateral Oophorectomy + Omentectomy + Hysterectomy | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| All patients | 1980 | 100.0% | 115 | 5.8% | 504 | 25.5% | 201 | 10.2% | 1160 | 58.6% | |
| Age at diagnosis (y) | | | | | | | | | | | |
| Younger than 45 | 377 | 19.0% | 13 | 11.3% | 86 | 17.1% | 54 | 26.9% | 224 | 19.3% | |
| 45-54 | 571 | 28.8% | 20 | 17.4% | 159 | 31.6% | 27 | 13.4% | 365 | 31.5% | |
| 55-69 | 732 | 37.0% | 43 | 37.4% | 193 | 38.3% | 72 | 35.8% | 424 | 36.6% | |
| 70 or older | 300 | 15.2% | 39 | 33.9% | 66 | 13.1% | 48 | 23.9% | 147 | 12.7% | |
| Mean+SD | 55.6±12.8 | | 61.6±14.0 | | 55.7±11.7 | | 55.1±18.0 | | 55.1±11.9 | | |
| Median (range) | 55 | (18-88) | 64 | (25-86) | 55 | (24-88) | 59 | (18-88) | 54 | (22-88) | <0.001 |
| Race / Ethnicity | | | | | | | | | | | |
| Non-Hispanic white | 1296 | 65.5% | 78 | 67.8% | 330 | 65.5% | 129 | 64.2% | 759 | 65.4% | |
| Non-Hispanic black | 64 | 3.2% | 7 | 6.1% | 17 | 3.4% | 12 | 6.0% | 28 | 2.4% | |
| Hispanic | 342 | 17.3% | 18 | 15.7% | 95 | 18.9% | 40 | 19.9% | 189 | 16.3% | |
| Asian/Pacific Islander | 278 | 14.0% | 12 | 10.4% | 62 | 12.3% | 20 | 10.0% | 184 | 15.9% | 0.019 |
| SES | | | | | | | | | | | |
| Lowest SES | 262 | 13.2% | 12 | 10.4% | 77 | 15.3% | 22 | 11.0% | 151 | 13.0% | |
| Lower-middle SES | 332 | 16.8% | 25 | 21.7% | 88 | 17.5% | 43 | 21.4% | 176 | 15.2% | |
| Middle SES | 415 | 21.0% | 30 | 26.1% | 107 | 21.2% | 43 | 21.4% | 235 | 20.3% | |
| Higher-middle SES | 459 | 23.2% | 28 | 24.4% | 118 | 23.4% | 46 | 22.9% | 267 | 23.0% | |
| Highest SES | 512 | 25.9% | 20 | 17.4% | 114 | 22.6% | 47 | 23.4% | 331 | 28.5% | 0.066 |
| Stage / Extension | | | | | | | | | | | |
| Regional, direct extension only | 1712 | 86.5% | 101 | 87.8% | 438 | 86.9% | 166 | 82.6% | 1007 | 86.8% | |
| Regional, lymph nodes only or both direct extension and lymph nodes | 268 | 13.5% | 14 | 12.2% | 66 | 13.1% | 35 | 17.4% | 153 | 13.2% | 0.397 |
| Tumor size | | | | | | | | | | | |
| <5cm | 202 | 10.2% | 16 | 13.9% | 58 | 11.5% | 17 | 8.5% | 111 | 9.6% | |
| 5-10cm | 502 | 25.4% | 30 | 26.1% | 118 | 23.4% | 45 | 22.4% | 309 | 26.6% | |
| 10cm+ | 751 | 37.9% | 36 | 31.3% | 175 | 34.7% | 91 | 45.3% | 449 | 38.7% | |
| Unknown | 525 | 26.5% | 33 | 28.7% | 153 | 30.4% | 48 | 23.9% | 291 | 25.1% | 0.070 |
| Grade | | | | | | | | | | | |
| Grade I | 222 | 11.2% | 10 | 8.7% | 62 | 12.3% | 24 | 11.9% | 126 | 10.9% | |
| Grade II | 525 | 26.5% | 28 | 24.4% | 132 | 26.2% | 52 | 25.9% | 313 | 27.0% | |
| Grade III | 669 | 33.8% | 33 | 28.7% | 166 | 32.9% | 70 | 34.8% | 400 | 34.5% | |
| Grade IV | 207 | 10.5% | 16 | 13.9% | 48 | 9.5% | 17 | 8.5% | 126 | 10.9% | |
| Not stated | 357 | 18.0% | 28 | 24.4% | 96 | 19.1% | 38 | 18.9% | 196 | 16.8% | 0.656 |

**Table 4.2 Early Stage Epithelial Ovarian Cancer Patient Race/Ethnicity Stratified by Socioeconomic Status Quintiles**

| Race / Ethnicity | Lowest SES | | Lower-middle SES | | Middle SES | | Higher-middle SES | | Highest SES | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-Hispanic white | 97 | 37.0% | 198 | 59.6% | 275 | 66.3% | 325 | 70.8% | 401 | 78.3% | |
| Non-Hispanic black | 21 | 8.0% | 17 | 5.1% | 11 | 2.7% | 9 | 2.0% | 6 | 1.2% | |
| Hispanic | 119 | 45.4% | 65 | 19.6% | 77 | 18.6% | 49 | 10.7% | 32 | 6.3% | |
| Asian/Pacific Islander | 25 | 9.5% | 52 | 15.7% | 52 | 12.5% | 76 | 16.6% | 73 | 14.3% | <0.001 |

To examine the independent effect of each characteristic on surgery type selection, we performed multinomial logistic regression using patients with the simplest surgery (Group 1) as the reference group. For each independent variable, we used the most common subgroup as the reference. Table 4.3 shows the results of the multinomial logistic regression. Patients diagnosed at 45-54 years old were significantly more likely to be Group 2 (OR 1.81, 95% CI 1.02-3.23) or Group 4 (OR 1.90, 95% CI 1.09-3.32). Patients diagnosed at 70 years or older were significantly less likely to be Group 2 (OR 0.38, 95% CI 0.22-0.63) or Group 4 (OR 0.38, 95% CI 0.23-0.61) than the patients diagnosed earlier. Patients diagnosed less than 45 years old were significantly more likely to be Group 3 (OR 2.66, 95% CI 1.28-5.53). Non-Hispanic black females were significantly less likely to be Group 4 (OR 0.33, 95% CI 0.13-0.83) than the non-Hispanic white females. Other than that, patients with lower-middle or middle SES were significantly less likely to be Group 4 (OR 0.42, 95% CI 0.22-0.80; OR 0.49, 95% CI 0.27-0.89) than the highest SES patients. Patients with a tumor smaller than 5cm were significantly less likely to be Group 3 (OR 0.42, 95% CI 0.19-0.94) than the patients with a larger tumor.

Then we wanted to examine the independent effect of each characteristic on surgery type selection using the most complicated surgery (Group 4) as the reference group. Again, for each independent variable, we used the most common subgroup as the reference. Table 4.4 shows the results of the multinomial logistic regression. Since we already compared Group 1 with Group 4,

this analysis would focus on the comparisons between the other groups. Non-Hispanic black patients were more likely to be Group 3 (OR 3.03, 95% CI 1.45-6.33) than the non-Hispanic white patients. Similarly, patients diagnosed at 70 years or older were significantly more likely to be Group 3 (OR 2.02, 95% CI 1.33-3.07) than the patients diagnosed earlier. Patients with lower-middle SES were significantly more likely to be Group 2 (OR 1.48, 95% CI 1.05-2.07) than the patients with the highest SES.

**Table 4.3 Multinomial Logistic Regression Analysis of Characteristics Associated with Early Stage Epithelial Ovarian Cancer Surgery Type Selection Using Patients with Bilateral (salpingo-) Oophorectomy Only as Reference Group.**

| Characteristics | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | | Group 4 Bilateral Oophorectomy + Hysterectomy + Omentectomy | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Age at diagnosis (y) | | | | | | |
| Younger than 45 | 1.54 | (0.78-3.06) | 2.66 | (1.28-5.53)* | 1.91 | (0.99-3.69) |
| 45-54 | 1.81 | (1.02-3.23)* | 0.82 | (0.41-1.66) | 1.90 | (1.09-3.32)* |
| 55-69 | 1.00 | | 1.00 | | 1.00 | |
| 70 or older | 0.38 | (0.22-0.63)* | 0.76 | (0.43-1.36) | 0.38 | (0.23-0.61)* |
| Race / Ethnicity | | | | | | |
| Non-Hispanic white | 1.00 | | 1.00 | | 1.00 | |
| Non-Hispanic black | 0.43 | (0.17-1.13) | 1.01 | (0.36-2.81) | 0.33 | (0.13-0.83)* |
| Hispanic | 1.01 | (0.56-1.84) | 1.21 | (0.63-2.36) | 0.94 | (0.53-1.66) |
| Asian/Pacific Islander | 1.03 | (0.52-2.03) | 0.92 | (0.42-2.01) | 1.35 | (0.71-2.58) |
| SES | | | | | | |
| Lowest SES | 1.07 | (0.47-2.43) | 0.60 | (0.24-1.51) | 0.75 | (0.34-1.65) |
| Lower-middle SES | 0.62 | (0.32-1.21) | 0.61 | (0.29-1.28) | 0.42 | (0.22-0.80)* |
| Middle SES | 0.64 | (0.34-1.22) | 0.54 | (0.26-1.10) | 0.49 | (0.27-0.89)* |
| Higher-middle SES | 0.76 | (0.40-1.44) | 0.67 | (0.33-1.37) | 0.59 | (0.32-1.07) |
| Highest SES | 1.00 | | 1.00 | | 1.00 | |
| Stage / Extension | | | | | | |
| Regional, direct extension only | 1.00 | | 1.00 | | 1.00 | |
| Regional, lymph nodes only or both direct extension and lymph nodes | 1.18 | (0.63-2.22) | 1.58 | (0.80-3.13) | 1.17 | (0.64-2.14) |
| Tumor size | | | | | | |
| <5cm | 0.80 | (0.41-1.57) | 0.42 | (0.19-0.94)* | 0.57 | (0.30-1.09) |
| 5-10cm | 0.82 | (0.47-1.42) | 0.58 | (0.32-1.08) | 0.80 | (0.48-1.35) |
| 10cm+ | 1.00 | | 1.00 | | 1.00 | |
| Unknown | 0.95 | (0.56-1.61) | 0.57 | (0.32-1.03) | 0.68 | (0.41-1.13) |
| Grade | | | | | | |
| Grade I | 0.96 | (0.44-2.11) | 0.93 | (0.39-2.22) | 0.79 | (0.37-1.68) |
| Grade II | 0.87 | (0.49-1.53) | 0.85 | (0.46-1.60) | 0.86 | (0.50-1.48) |
| Grade III | 1.00 | | 1.00 | | 1.00 | |
| Grade IV | 0.63 | (0.31-1.26) | 0.51 | (0.23-1.14) | 0.66 | (0.35-1.27) |
| Not stated | 0.53 | (0.30-0.96)* | 0.54 | (0.28-1.04) | 0.44 | (0.25-0.76)* |

* $p<0.05$.

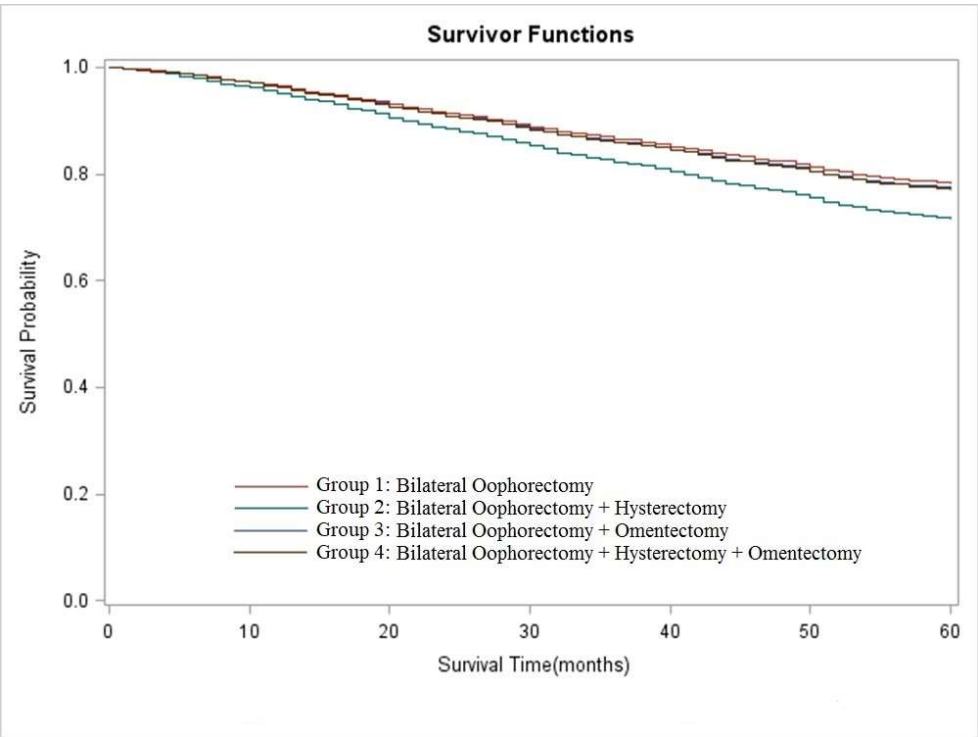
**Table 4.4 Multinomial Logistic Regression Analysis of Characteristics Associated with Early Stage Epithelial Ovarian Cancer Surgery Type Selection Using Patients With Complete Surgery as Reference Group**

| Characteristics | Group 1 Bilateral Oophorectomy | | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Age at diagnosis (y) | | | | | | |
| Younger than 45 | 0.52 | (0.27-1.01) | 0.81 | (0.59-1.10) | 1.39 | (0.92-2.09) |
| 45-54 | 0.53 | (0.30-0.92)* | 0.96 | (0.74-1.24) | 0.43 | (0.27-0.69)* |
| 55-69 | 1.00 | | 1.00 | | 1.00 | |
| 70 or older | 2.66 | (1.64-4.31)* | 1.00 | (0.71-1.40) | 2.02 | (1.33-3.07)* |
| Race / Ethnicity | | | | | | |
| Non-Hispanic white | 1.00 | | 1.00 | | 1.00 | |
| Non-Hispanic black | 3.00 | (1.21-7.47)* | 1.30 | (0.69-2.44) | 3.03 | (1.45-6.33)* |
| Hispanic | 1.07 | (0.60-1.89) | 1.08 | (0.80-1.46) | 1.29 | (0.84-1.98) |
| Asian/Pacific Islander | 0.74 | (0.39-1.41) | 0.76 | (0.55-1.05) | 0.68 | (0.41-1.13) |
| SES | | | | | | |
| Lowest SES | 1.33 | (0.61-2.94) | 1.43 | (0.98-2.07) | 0.79 | (0.44-1.42) |
| Lower-middle SES | 2.38 | (1.26-4.50)* | 1.48 | (1.05-2.07)* | 1.45 | (0.90-2.31) |
| Middle SES | 2.06 | (1.12-3.78)* | 1.32 | (0.96-1.82) | 1.11 | (0.70-1.75) |
| Higher-middle SES | 1.71 | (0.93-3.14) | 1.30 | (0.96-1.77) | 1.15 | (0.74-1.79) |
| Highest SES | 1.00 | | 1.00 | | 1.00 | |
| Stage / Extension | | | | | | |
| Regional, direct extension only | 1.00 | | 1.00 | | 1.00 | |
| Regional, lymph nodes only or both direct extension and lymph nodes | 0.85 | (0.47-1.56) | 1.01 | (0.74-1.38) | 1.35 | (0.89-2.04) |
| Tumor size | | | | | | |
| <5cm | 1.75 | (0.92-3.33) | 1.40 | (0.97-2.02) | 0.74 | (0.42-1.31) |
| 5-10cm | 1.25 | (0.74-2.10) | 1.03 | (0.78-1.36) | 0.73 | (0.49-1.08) |
| 10cm+ | 1.00 | | 1.00 | | 1.00 | |
| Unknown | 1.47 | (0.88-2.43) | 1.39 | (1.07-1.81)* | 0.84 | (0.57-1.23) |
| Grade | | | | | | |
| Grade I | 1.27 | (0.60-2.71) | 1.23 | (0.85-1.76) | 1.19 | (0.70-2.01) |
| Grade II | 1.16 | (0.68-1.99) | 1.01 | (0.77-1.33) | 0.99 | (0.66-1.48) |
| Grade III | 1.00 | | 1.00 | | 1.00 | |
| Grade IV | 1.51 | (0.79-2.90) | 0.95 | (0.65-1.40) | 0.77 | (0.43-1.37) |
| Not stated | 2.28 | (1.31-3.97)* | 1.22 | (0.89-1.66) | 1.23 | (0.79-1.92) |

* $p<0.05$.

Kaplan-Meier survival analysis (Figure 4.1) revealed that Group 2 early stage EOC patients had the lowest five-year survival rate (71.6%). The five-year survival rates for Group 1, Group 3, and Group 4 were 78.2%, 77.4%, and 77.1% respectively.

**Figure 4.1 Five-year Survival of Early Stage Epithelial Ovarian Cancer Patients by Surgery Types**




Multivariable survival analysis using the simplest surgery (Group 1) or the most complicated surgery (Group 4) as the reference group revealed that Group 2 had a significantly adverse effect on early stage EOC five-year survival (HR 1.29, 95% CI 1.04-1.58) compared with Group 4 (Table 4.5 & Table 4.6). Younger age at diagnosis (<45 years old, OR 0.63, 95% CI 0.47-0.85) and lower tumor grade (Grade I, OR 0.51, 95% CI 0.34-0.75; Grade II, OR 0.69, 95% CI 0.54-0.89) showed protective effects on early stage EOC five-year survival. However, being diagnosed at older age (70 years or older, OR 1.58, 95% CI 1.24-2.01), having lower SES (lower-middle SES, OR 1.33, 95% CI 1.01-1.74), and having lymph node involvement (OR 1.72, 95% CI 1.37-2.15) were associated with significantly increased risk of death.

## Table 4.5 Unadjusted Cox Proportional Hazard Regression Analysis of Early Stage Epithelial Ovarian Cancer Surgery Types

| | Reference Group | Parameter Estimate | Std | Chi-Square | p > ChiSq | HR | 95% CI |
|---|---|---|---|---|---|---|---|
| Group 1: Bilateral Oophorectomy | Group 1 | | | | | 1.00 | |
| | Group 4 | 0.158 | 0.196 | 0.65 | 0.420 | 1.17 | (0.80-1.72) |
| Group 2: Bilateral Oophorectomy + Hysterectomy | Group 1 | 0.096 | 0.204 | 0.22 | 0.640 | 1.10 | (0.74-1.64) |
| | Group 4 | 0.254 | 0.106 | 5.73 | 0.017 | 1.29 | (1.05-1.59)* |
| Group 3: Bilateral Oophorectomy + Omentectomy | Group 1 | -0.090 | 0.236 | 0.14 | 0.704 | 0.91 | (0.56-1.45) |
| | Group 4 | 0.068 | 0.159 | 0.19 | 0.667 | 1.07 | (0.78-1.46) |
| Group 4: Bilateral Oophorectomy + Hysterectomy + Omentectomy | Group 1 | -0.158 | 0.196 | 0.65 | 0.420 | 0.85 | (0.58-1.25) |
| | Group 4 | | | | | 1.00 | |

* p<0.05.

## Table 4.6 Adjusted Cox Proportional Hazard Regression Analysis of Early Stage Epithelial Ovarian Cancer Surgery Types

| | Reference Group | Parameter Estimate | Std | Chi-Square | p > ChiSq | HR | 95% CI |
|---|---|---|---|---|---|---|---|
| Surgery Type | | | | | | | |
| Group 1: Bilateral Oophorectomy | Group 1 | | | | | 1.00 | |
| | Group 4 | -0.057 | 0.199 | 0.08 | 0.776 | 0.95 | (0.64-1.40) |
| Group 2: Bilateral Oophorectomy + Hysterectomy | Group 1 | 0.308 | 0.207 | 2.21 | 0.137 | 1.36 | (0.91-2.04) |
| | Group 4 | 0.215 | 0.106 | 5.58 | 0.018 | 1.29 | (1.04-1.58)* |
| Group 3: Bilateral Oophorectomy + Omentectomy | Group 1 | 0.045 | 0.238 | 0.04 | 0.851 | 1.05 | (0.66-1.67) |
| | Group 4 | -0.012 | 0.161 | 0.01 | 0.939 | 0.99 | (0.72-1.36) |
| Group 4: Bilateral Oophorectomy + Hysterectomy + Omentectomy | Group 1 | 0.057 | 0.199 | 0.08 | 0.776 | 1.06 | (0.72-1.56) |
| | Group 4 | | | | | 1.00 | |
| Age at diagnosis (y) | | | | | | | |
| Younger than 45 | | -0.460 | 0.151 | 9.24 | 0.002 | 0.63 | (0.47-0.85)* |
| 45-54 | | -0.191 | 0.120 | 2.54 | 0.111 | 0.83 | (0.65-1.05) |
| 55-69 | | | | | | 1.00 | |
| 70 or older | | 0.457 | 0.122 | 13.98 | <0.001 | 1.58 | (1.24-2.01)* |
| SES | | | | | | | |
| Lowest SES | | 0.201 | 0.158 | 1.62 | 0.204 | 1.22 | (0.90-1.67) |
| Lower-middle SES | | 0.281 | 0.140 | 4.03 | 0.045 | 1.33 | (1.01-1.74)* |
| Middle SES | | -0.100 | 0.141 | 0.50 | 0.481 | 0.91 | (0.69-1.19) |
| Higher-middle SES | | 0.006 | 0.135 | <0.01 | 0.963 | 1.01 | (0.77-1.31) |
| Highest SES | | | | | | 1.00 | |
| Stage | | | | | | | |
| Regional, direct extension only | | | | | | 1.00 | |
| Regional, lymph nodes only or both direct extension and lymph nodes | | 0.540 | 0.116 | 21.55 | <0.001 | 1.72 | (1.37-2.15)* |
| Grade | | | | | | | |
| Grade I | | -0.683 | 0.205 | 11.13 | <0.001 | 0.51 | (0.34-0.75)* |
| Grade II | | -0.369 | 0.127 | 8.51 | 0.004 | 0.69 | (0.54-0.89)* |
| Grade III | | | | | | 1.00 | |
| Grade IV | | 0.254 | 0.140 | 3.30 | 0.069 | 1.29 | (0.98-1.70) |
| Not stated | | -0.047 | 0.133 | 0.13 | 0.723 | 0.95 | (0.74-1.24) |

* p<0.05.

4.2 Advanced Stage Epithelial Ovarian Cancer

5,725 advanced stage EOC patients diagnosed between 1988 and 2008 were included in this study (Table 4.7). The median age at diagnosis was 60 years old (range 18–94 years old) with a mean of 59.2 years old (±13.2 years old). 70.9% (4,058) subjects were non-Hispanic white females. Most patients had higher SES (higher-middle, 1,332, 23.3%; highest, 1,370, 23.9%). Most patients with known tumor size had a tumor larger than 10cm (1,228, 21.5%). 47.8% (2,735) patients had a grade III tumor which was poorly differentiated.

Overall, 263(4.6%) advanced stage EOC patients received bilateral (salpingo-) oophorectomy as the only surgery (Group 1), 832 (14.5%) patients received bilateral (salpingo-) oophorectomy with hysterectomy (Group 2), 1,042(18.2%) received bilateral (salpingo-) oophorectomy with omentectomy (Group 3), and 3,588 (62.7%) received complete surgery: bilateral (salpingo-) oophorectomy with omentectomy and hysterectomy (Group 4).

According to Pearson chi-square result, age at diagnosis, race/ethnicity, and tumor size were statistically significantly ($p<0.05$) associated with surgery type selection. Patients diagnosed at 45-54 years old were more likely to be Group 2 (241, 29.0%). Most patients in Group 1 were diagnosed at 70 years or older (108, 41.1%). Unlike non-Hispanic white females who were more likely to be Group 3 (811, 77.8%) than Group 2 (554, 66.6%), fewer Asian/Pacific Islander patients were in Group 3 (53, 5.1%) than in Group 2 (94, 11.3%).

As shown in Table 4.8, we noticed that race/ethnicity was associated with socioeconomic status (SES, $p<0.05$). Most patients with the highest SES were non-Hispanic white (1,116, 81.5%). Non-Hispanic black and Hispanic patients were more likely to have the lowest SES (69, 8.8%; 295, 37.5%).

## Table 4.7 Advanced Stage Epithelial Ovarian Cancer Patient Characteristics

| Characteristics | All | | Group 1 Bilateral Oophorectomy | | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | | Group 4 Bilateral Oophorectomy + Omentectomy + Hysterectomy | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| All patients | 5725 | 100.0% | 263 | 4.6% | 832 | 14.5% | 1042 | 18.2% | 3588 | 62.7% | |
| Age at diagnosis (y) | | | | | | | | | | | |
| Younger than 45 | 802 | 14.0% | 22 | 8.4% | 127 | 15.3% | 88 | 8.5% | 565 | 15.8% | |
| 45-54 | 1266 | 22.1% | 36 | 13.7% | 241 | 29.0% | 139 | 13.3% | 850 | 23.7% | |
| 55-69 | 2251 | 39.3% | 97 | 36.9% | 300 | 36.1% | 458 | 44.0% | 1396 | 38.9% | |
| 70 or older | 1406 | 24.6% | 108 | 41.1% | 164 | 19.7% | 357 | 34.3% | 777 | 21.7% | <0.001 |
| Mean+SD | 59.2±13.2 | | 63.9±12.8 | | 57.6±12.8 | | 62.9±13.4 | | 58.2±13.0 | | |
| Median (range) | 60 | (18-94) | 66 | (18-88) | 57 | (19-88) | 65 | (18-91) | 58.5 | (18-94) | |
| Race | | | | | | | | | | | |
| Non-Hispanic white | 4058 | 70.9% | 191 | 72.6% | 554 | 66.6% | 811 | 77.8% | 2502 | 69.7% | |
| Non-Hispanic black | 244 | 4.3% | 12 | 4.6% | 43 | 5.2% | 42 | 4.0% | 147 | 4.1% | |
| Hispanic | 912 | 15.9% | 47 | 17.9% | 141 | 17.0% | 136 | 13.1% | 588 | 16.4% | |
| Asian/Pacific Islander | 511 | 8.9% | 13 | 4.9% | 94 | 11.3% | 53 | 5.1% | 351 | 9.8% | <0.001 |
| SES | | | | | | | | | | | |
| Lowest SES | 787 | 13.8% | 39 | 14.8% | 123 | 14.8% | 135 | 13.0% | 490 | 13.7% | |
| Lower-middle SES | 1043 | 18.2% | 42 | 16.0% | 169 | 20.3% | 194 | 18.6% | 638 | 17.8% | |
| Middle SES | 1193 | 20.8% | 58 | 22.1% | 160 | 19.2% | 226 | 21.7% | 749 | 20.9% | |
| Higher-middle SES | 1332 | 23.3% | 63 | 24.0% | 199 | 23.9% | 232 | 22.3% | 838 | 23.4% | |
| Highest SES | 1370 | 23.9% | 61 | 23.2% | 181 | 21.8% | 255 | 24.5% | 873 | 24.3% | 0.712 |
| Stage | | | | | | | | | | | |
| Distant | 5725 | 100.0% | 263 | 4.6% | 832 | 14.5% | 1042 | 18.2% | 3588 | 62.7% | |
| Tumor size | | | | | | | | | | | |
| <5cm | 643 | 11.2% | 43 | 16.4% | 81 | 9.7% | 124 | 11.9% | 395 | 11.0% | |
| 5-10cm | 1208 | 21.1% | 47 | 17.9% | 190 | 22.8% | 220 | 21.1% | 751 | 20.9% | |
| 10cm+ | 1228 | 21.5% | 42 | 16.0% | 180 | 21.6% | 192 | 18.4% | 814 | 22.7% | |
| Unknown | 2646 | 46.2% | 131 | 49.8% | 381 | 45.8% | 506 | 48.6% | 1628 | 45.4% | 0.004 |
| Grade | | | | | | | | | | | |
| Grade I | 324 | 5.7% | 9 | 3.4% | 49 | 5.9% | 59 | 5.7% | 207 | 5.8% | |
| Grade II | 1081 | 18.9% | 47 | 17.9% | 144 | 17.3% | 194 | 18.6% | 696 | 19.4% | |
| Grade III | 2735 | 47.8% | 131 | 49.8% | 375 | 45.1% | 519 | 49.8% | 1710 | 47.7% | |
| Grade IV | 579 | 10.1% | 25 | 9.5% | 88 | 10.6% | 99 | 9.5% | 367 | 10.2% | |
| Not stated | 1006 | 17.6% | 51 | 19.4% | 176 | 21.2% | 171 | 16.4% | 608 | 17.0% | 0.213 |

**Table 4.8 Advanced Stage Epithelial Ovarian Cancer Patient Race/Ethnicity Stratified by Socioeconomic Status Quintile**

| Race / Ethnicity | Lowest SES | | Lower-middle SES | | Middle SES | | Higher-middle SES | | Highest SES | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-Hispanic white | 355 | 45.1% | 684 | 65.6% | 871 | 73.0% | 1032 | 77.5% | 1116 | 81.5% | |
| Non-Hispanic black | 69 | 8.8% | 61 | 5.9% | 47 | 3.9% | 41 | 3.1% | 26 | 1.9% | |
| Hispanic | 295 | 37.5% | 221 | 21.2% | 172 | 14.4% | 130 | 9.8% | 94 | 6.9% | |
| Asian/Pacific Islander | 68 | 8.6% | 77 | 7.4% | 103 | 8.6% | 129 | 9.7% | 134 | 9.8% | <0.001 |

To examine the independent effect of each characteristic on surgery type selection, we performed multinomial logistic regression using patients with the simplest surgery (Group 1) as the reference group. For each independent variable, we used the most common subgroup as the reference. Table 4.9 shows the results of the multinomial logistic regression. Patients who were diagnosed before 55 years old were more likely to be Group 2 (<45 years old, OR 1.77, 95% CI 1.06-2.96; 45-54 years old, OR 2.09, 95% CI 1.37-3.19) or Group 4 (<45 years old, OR 1.72, 95% CI 1.06-2.77; 45-54 years old, OR 1.59, 95% CI 1.07-2.36). Patients diagnosed at 70 or older were less likely to be Group 2 (OR 0.49, 95% CI 0.35-0.69), Group 3 (OR 0.68, 95% CI 0.50-0.93), or Group 4 (OR 0.50, 95% CI 0.37-0.67). Asian/Pacific Islander patients were more likely to be Group 2 (OR 1.88, 95% CI 1.02-3.46) than non-Hispanic white patients. Hispanic patients were less likely to be Group 3 (OR 0.65, 95% CI 0.44-0.96). Patients with a tumor less than 5cm were less likely to be Group 2 (OR 0.50, 95% CI 0.30-0.83), Group 3 (OR 0.63, 95% CI 0.39-1.02), or Group 4 (OR 0.52, 95% CI 0.33-0.81) compared with the reference group.

Then we wanted to examine the independent effect of each characteristic on surgery type selection using the most complicated surgery (Group 4) as the reference group. Again, for each independent variable, we used the most common subgroup as the reference. Table 4.10 shows the results of the multinomial logistic regression. Since we already compared Group 1 with the Group 4, this analysis would focus on the comparisons of the other groups. Younger patients were less likely to be Group 3 (<45 years old, OR 0.50, 95% CI 0.39-0.64; 45-54 years old, OR

0.52, 95% CI 0.42-0.64) than Group 4. Patients diagnosed at 45-54 years old were more likely to be Group 2 (OR 1.32, 95% CI 1.09-1.59). Patients diagnosed at 70 years or older were more likely to be Group 3 (OR 1.36, 95% CI 1.15-1.60). Asian/Pacific Islander females were less likely to be Group 3 (OR 0.57, 95% CI 0.42-0.77) than non-Hispanic white females.

**Table 4.9 Multinomial Logistic Regression Analysis of Characteristics Associated with Advanced Stage Epithelial Ovarian Cancer Surgery Type Selection Using Patients with Bilateral (salpingo-) Oophorectomy Only as Reference Group**

| Characteristics | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | | Group 4 Bilateral Oophorectomy + Hysterectomy + Omentectomy | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Age at diagnosis (y) | | | | | | |
| Younger than 45 | 1.77 | (1.06-2.96)* | 0.85 | (0.51-1.44) | 1.72 | (1.06-2.77)* |
| 45-54 | 2.09 | (1.37-3.19)* | 0.82 | (0.53-1.26) | 1.59 | (1.07-2.36)* |
| 55-69 | 1.00 | | 1.00 | | 1.00 | |
| 70 or older | 0.49 | (0.35-0.69)* | 0.68 | (0.50-0.93)* | 0.50 | (0.37-0.67)* |
| Race / Ethnicity | | | | | | |
| Non-Hispanic white | 1.00 | | 1.00 | | 1.00 | |
| Non-Hispanic black | 1.01 | (0.51-1.99) | 0.80 | (0.41-1.57) | 0.81 | (0.43-1.50) |
| Hispanic | 0.77 | (0.52-1.14) | 0.65 | (0.44-0.96)* | 0.77 | (0.54-1.10) |
| Asian/Pacific Islander | 1.88 | (1.02-3.46)* | 0.93 | (0.49-1.75) | 1.65 | (0.92-2.94) |
| SES | | | | | | |
| Lowest SES | 1.03 | (0.63-1.67) | 0.94 | (0.58-1.50) | 0.88 | (0.57-1.36) |
| Lower-middle SES | 1.42 | (0.90-2.24) | 1.19 | (0.77-1.85) | 1.11 | (0.74-1.68) |
| Middle SES | 0.89 | (0.58-1.36) | 0.95 | (0.63-1.42) | 0.87 | (0.60-1.27) |
| Higher-middle SES | 1.06 | (0.70-1.60) | 0.90 | (0.61-1.34) | 0.94 | (0.65-1.36) |
| Highest SES | 1.00 | | 1.00 | | | |
| Tumor size | | | | | | |
| <5cm | 0.50 | (0.30-0.83)* | 0.63 | (0.39-1.02) | 0.52 | (0.33-0.81)* |
| 5-10cm | 1.04 | (0.65-1.66) | 1.03 | (0.65-1.64) | 0.88 | (0.57-1.36) |
| 10cm+ | 1.00 | | 1.00 | | 1.00 | |
| Unknown | 0.76 | (0.52-1.13) | 0.86 | (0.58-1.26) | 0.71 | (0.49-1.01) |
| Grade | | | | | | |
| Grade I | 1.58 | (0.75-3.33) | 1.68 | (0.81-3.49) | 1.45 | (0.72-2.92) |
| Grade II | 1.00 | (0.68-1.47) | 1.03 | (0.71-1.50) | 1.06 | (0.75-1.50) |
| Grade III | 1.00 | | 1.00 | | 1.00 | |
| Grade IV | 1.20 | (0.73-1.96) | 1.00 | (0.62-1.61) | 1.09 | (0.70-1.71) |
| Not stated | 1.19 | (0.82-1.73) | 0.87 | (0.60-1.26) | 0.90 | (0.64-1.27) |

* $p<0.05$.

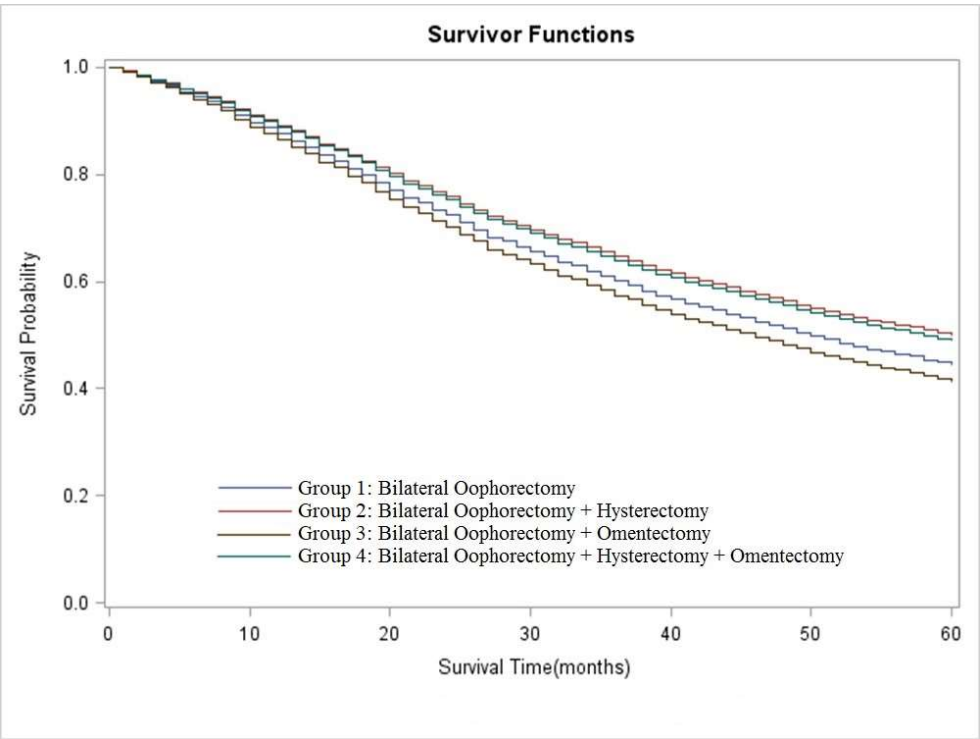
**Table 4.10 Multinomial Logistic Regression Analysis of Characteristics Associated with Advanced Stage Epithelial Ovarian Cancer Surgery Type Selection Using Patients with Complete Surgery as Reference Group**

| Characteristics | Group 1 Bilateral Oophorectomy | | Group 2 Bilateral Oophorectomy + Hysterectomy | | Group 3 Bilateral Oophorectomy + Omentectomy | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Age at diagnosis (y) | | | | | | |
| Younger than 45 | 0.58 | (0.36-0.94)* | 1.03 | (0.81-1.30) | 0.50 | (0.39-0.64)* |
| 45-54 | 0.63 | (0.42-0.93)* | 1.32 | (1.09-1.59)* | 0.52 | (0.42-0.64)* |
| 55-69 | 1.00 | | 1.00 | | 1.00 | |
| 70 or older | 2.00 | (1.50-2.68)* | 0.98 | (0.80-1.21) | 1.36 | (1.15-1.60)* |
| Race | | | | | | |
| Non-Hispanic white | 1.00 | | 1.00 | | 1.00 | |
| Non-Hispanic black | 1.24 | (0.67-2.31) | 1.25 | (0.88-1.79) | 0.99 | (0.69-1.43) |
| Hispanic | 1.30 | (0.91-1.85) | 1.00 | (0.80-1.24) | 0.84 | (0.68-1.04) |
| Asian/Pacific Islander | 0.61 | (0.34-1.08) | 1.14 | (0.89-1.46) | 0.57 | (0.42-0.77)* |
| SES | | | | | | |
| Lowest SES | 1.14 | (0.74-1.77) | 1.17 | (0.90-1.53) | 1.07 | (0.83-1.37) |
| Lower-middle SES | 0.90 | (0.59-1.36) | 1.28 | (1.01-1.62)* | 1.07 | (0.86-1.33) |
| Middle SES | 1.15 | (0.79-1.67) | 1.02 | (0.80-1.29) | 1.09 | (0.88-1.34) |
| Higher-middle SES | 1.07 | (0.74-1.54) | 1.13 | (0.90-1.41) | 0.96 | (0.78-1.18) |
| Highest SES | 1.00 | | 1.00 | | 1.00 | |
| Tumor size | | | | | | |
| <5cm | 1.93 | (1.24-3.02)* | 0.96 | (0.72-1.29) | 1.22 | (0.94-1.58) |
| 5-10cm | 1.13 | (0.73-1.74) | 1.18 | (0.94-1.48) | 1.17 | (0.94-1.46) |
| 10cm+ | 1.00 | | 1.00 | | 1.00 | |
| Unknown | 1.42 | (0.99-2.03) | 1.08 | (0.89-1.32) | 1.21 | (1.00-1.47)* |
| Grade | | | | | | |
| Grade I | 0.69 | (0.34-1.39) | 1.09 | (0.78-1.52) | 1.16 | (0.84-1.58) |
| Grade II | 0.94 | (0.67-1.33) | 0.94 | (0.76-1.16) | 0.97 | (0.81-1.18) |
| Grade III | 1.00 | | 1.00 | | 1.00 | |
| Grade IV | 0.92 | (0.59-1.43) | 1.10 | (0.85-1.42) | 0.91 | (0.71-1.17) |
| Not stated | 1.11 | (0.79-1.56) | 1.32 | (1.08-1.61)* | 0.97 | (0.79-1.18) |

* $p<0.05$.

Kaplan-Meier survival analysis (Figure 4.2) revealed that Group 3 advanced stage EOC patients had the lowest five-year survival rate (41.3%). The five-year survival rates for the Group 1, Group 2, and Group 4 were 44.4%, 49.9%, and 48.9% respectively.

**Figure 4.2 Five-year Survival of Advanced Stage Epithelial Ovarian Cancer Patients by Surgery Types**




Multivariable survival analysis using the simplest surgery (Group 1) or the most complicated surgery (Group 4) as the reference group revealed that Group 2 had a protective effect on advanced stage EOC five-year survival compared with the Group 1 (Table 4.13 & Table 4.14). Even though not statistically significant, Group 2 had a decreased risk of death by about 14% (HR 0.86, 95% CI 0.72-1.02) compared with Group 1. Group 3 had about 24% significantly increased the risk of death (HR 1.24, 95% CI 1.14-1.35) than Group 4. Being diagnosed at younger age (<45 years old, HR 0.66, 95% CI 0.58-0.74; 45-54 years old, HR 0.83, 95% CI 0.76-0.91) or having lower grade tumor (Grade I, HR 0.42, 95% CI 0.35-0.52; Grade II, HR 0.81, 95% CI 0.74-0.89) showed a protective effect on advanced stage EOC five-year survival. However, being diagnosed late (70 years or older, HR 1.34, 95% CI 1.23-1.45), being

non-Hispanic black (HR 1.33, 95% CI 1.21-1.55), having lower SES (lowest, HR 1.26, 95% CI 1.12-1.41; lower-middle, HR 1.14, 95% CI 1.03-1.27; middle, HR 1.21, 95% CI 1.09-1.33), or having smaller tumor size (<5cm, HR 1.19, 95% CI 1.05-1.35; 5-10cm, HR 1.15, 95% CI 1.03-1.28) were associated with significantly higher risk of death.

**Table 4.11 Unadjusted Cox Proportional Hazard Regression Analysis of Advanced Stage Epithelial Ovarian Cancer Surgery Types**

| | Reference Group | Parameter Estimate | Std | Chi-Square | p > ChiSq | HR | 95% CI |
|---|---|---|---|---|---|---|---|
| Group 1: Bilateral Oophorectomy | Group 1 | | | | | 1.00 | |
| | Group 4 | 0.266 | 0.078 | 11.48 | <0.001 | 1.30 | (1.12-1.52)* |
| Group 2: Bilateral Oophorectomy + Hysterectomy | Group 1 | -0.290 | 0.088 | 10.80 | 0.001 | 0.75 | (0.63-0.89)* |
| | Group 4 | -0.024 | 0.051 | 0.22 | 0.636 | 0.98 | (0.88-1.08) |
| Group 3: Bilateral Oophorectomy + Omentectomy | Group 1 | 0.032 | 0.084 | 0.14 | 0.704 | 1.03 | (0.88-1.22) |
| | Group 4 | 0.298 | 0.043 | 47.25 | <0.001 | 1.35 | (1.24-1.47)* |
| Group 4: Bilateral Oophorectomy + Hysterectomy + Omentectomy | Group 1 | -0.266 | 0.078 | 11.48 | <0.001 | 0.77 | (0.66-0.89)* |
| | Group 4 | | | | | 1.00 | |

* p<0.05.

## Table 4.12 Adjusted Cox Proportional Hazard Regression Analysis of Advanced Stage Epithelial Ovarian Cancer Surgery Types

| | Reference Group | Parameter Estimate | Std | Chi-Square | p > ChiSq | HR | 95% CI |
|---|---|---|---|---|---|---|---|
| Surgery Type | | | | | | | |
| Group 1: Bilateral Oophorectomy | Group1 | | | | | 1.00 | |
| | Group 4 | 0.128 | 0.079 | 2.61 | 0.106 | 1.14 | (0.97-1.33) |
| Group 2: Bilateral Oophorectomy | Group 1 | -0.156 | 0.089 | 3.06 | 0.080 | 0.86 | (0.72-1.02) |
| + Hysterectomy | Group 4 | -0.028 | 0.051 | 0.30 | 0.583 | 0.97 | (0.88-1.07) |
| Group 3: Bilateral Oophorectomy | Group 1 | 0.085 | 0.084 | 1.02 | 0.312 | 1.09 | (0.92-1.29) |
| + Omentectomy | Group 4 | 0.213 | 0.044 | 23.62 | <0.001 | 1.24 | (1.14-1.35)* |
| Group 4: Bilateral Oophorectomy | Group 1 | -0.128 | 0.079 | 2.61 | 0.106 | 0.88 | (0.75-1.03) |
| + Hysterectomy + Omentectomy | Group 4 | | | | | 1.00 | |
| Age at diagnosis (y) | | | | | | | |
| Younger than 45 | | -0.423 | 0.062 | 46.92 | <0.001 | 0.66 | (0.58-0.74)* |
| 45-54 | | -0.194 | 0.047 | 15.31 | <0.001 | 0.83 | (0.76-0.91)* |
| 55-69 | | | | | | 1.00 | |
| 70 or older | | 0.291 | 0.041 | 49.58 | <0.001 | 1.34 | (1.23-1.45)* |
| Race | | | | | | | |
| Non-Hispanic white | | | | | | 1.00 | |
| Non-Hispanic black | | 0.281 | 0.081 | 12.06 | <0.001 | 1.33 | (1.13-1.55)* |
| Hispanic | | -0.037 | 0.051 | 0.52 | 0.472 | 0.96 | (0.87-1.07) |
| Asian/Pacific Islander | | -0.024 | 0.064 | 0.14 | 0.708 | 0.98 | (0.86-1.11) |
| SES | | | | | | | |
| Lowest SES | | 0.228 | 0.060 | 14.33 | <0.001 | 1.26 | (1.12-1.41)* |
| Lower-middle SES | | 0.132 | 0.054 | 6.06 | 0.014 | 1.14 | (1.03-1.27)* |
| Middle SES | | 0.187 | 0.051 | 13.402 | <0.001 | 1.21 | (1.09-1.33)* |
| Higher-middle SES | | 0.064 | 0.050 | 1.65 | 0.200 | 1.07 | (0.97-1.18) |
| Highest SES | | | | | | 1.00 | |
| Tumor size | | | | | | | |
| <5cm | | 0.171 | 0.065 | 7.00 | 0.008 | 1.19 | (1.05-1.35)* |
| 5-10cm | | 0.138 | 0.055 | 6.28 | 0.012 | 1.15 | (1.03-1.28)* |
| 10cm+ | | | | | | 1.00 | |
| Unknown | | 0.368 | 0.047 | 61.29 | <0.001 | 1.45 | (1.32-1.58)* |
| Grade | | | | | | | |
| Grade I | | -0.862 | 0.104 | 69.37 | <0.001 | 0.42 | (0.35-0.52)* |
| Grade II | | -0.208 | 0.048 | 19.01 | <0.001 | 0.81 | (0.74-0.89)* |
| Grade III | | | | | | 1.00 | |
| Grade IV | | 0.059 | 0.057 | 1.08 | 0.299 | 1.06 | (0.95-1.19) |
| Not stated | | -0.017 | 0.047 | 0.13 | 0.722 | 0.98 | (0.90-1.08) |

* p<0.05.

# CHAPTER 5

# DISCUSSION

## 5.1 Summary

Due to the large number of affected women and poor prognosis of epithelial ovarian cancer (EOC), improving the treatment methods for epithelial ovarian cancer patients becomes a research priority to increase survival length and post-surgical quality of life.

Among 1,980 early stage epithelial ovarian cancer (EOC) participants, 86.5% of them were diagnosed at regional stage with direct extension only. Most early stage EOC patients received complete surgery of bilateral (salpingo-) oophorectomy with omentectomy and hysterectomy. Our study found that patients who were diagnosed after 70 years old were more likely to receive bilateral (salpingo-) oophorectomy only, while patients who were diagnosed before 45 years old were more likely to undergo bilateral (salpingo-) oophorectomy with omentectomy. Few non-Hispanic black females received complete surgery, and this might relate to their socioeconomic status. Non-Hispanic black and Hispanic patients were more likely to have the lowest SES.

**Table 5.1 Summary of Results**

| Findings | Possible Explanations |
|---|---|
| Early Stage | |
| Bilateral Oophorectomy + Hysterectomy + **Omentectomy** (Group 4) | 1. Omentectomy is effective |
| > Bilateral Oophorectomy + Hysterectomy (Group 2) | 2. SES |
| | |
| Advanced Stage | |
| Bilateral Oophorectomy + **Hysterectomy** (Group 2) | 1. Hysterectomy is effective |
| > Bilateral Oophorectomy only (Group 1) | |
| | |
| Bilateral Oophorectomy + **Hysterectomy** + Omentectomy (Group 4) | 1. Hysterectomy is effective |
| > Bilateral Oophorectomy + Omentectomy (Group3) | |

Five-year survival rates of early stage epithelial ovarian cancer patients were higher than 70%. Survival analysis revealed that bilateral (salpingo-) oophorectomy with hysterectomy group had a significantly lower five-year survival rate compared with the complete surgery group. One possible explanation is that omentectomy might be effective in improving five-year EOC survival. However, patients who received bilateral (salpingo-) oophorectomy with omentectomy did not have better five-year survival rate compared with patients who received bilateral (salpingo-) oophorectomy only. Our finding is consistent with the results presented by McNally et al.[13] suggesting that omentectomy is not necessary for all early stage EOC patients as most of them do not have omental metastasis. As a result, omentectomy was not the determining factor of early stage EOC five-year survival. Another possible explanation is that the low five-year survival rate of bilateral (salpingo-) oophorectomy with hysterectomy group might be a result of relatively low socioeconomic status. The bilateral (salpingo-) oophorectomy with hysterectomy group consisted of more patients with the lowest or lower-middle socioeconomic status. Low socioeconomic status showed a significantly negative effect on early stage EOC five-year survival. Although not statistically significant, the five-year survival rate of bilateral (salpingo-) oophorectomy with hysterectomy group was lower than all other groups. This suggests that hysterectomy might not be necessary for all early stage EOC patients since there was less risk of uterine involvement at early stage[9]. Removing the structure without affect cells would not improve long-term survival. Other than that, patients who received complete surgery did not show significant improvement in five-year survival rate compared with the bilateral (salpingo-) oophorectomy only and the bilateral (salpingo-) oophorectomy with omentectomy groups. Considering the aggressiveness and the effectiveness, complete surgery might not be the best approach for early stage EOC patients. Although not statistically significantly different than

other groups, the simplest surgery group (bilateral (salpingo-) oophorectomy only) had the highest five-year survival rate.

We also included 5,725 advanced stage EOC patients in this study. Most of them received complete surgery (62.7%), and very few of them received bilateral (salpingo-) oophorectomy only (4.6%). Statistical analysis revealed that patients who were diagnosed after 70 years or older were more likely to receive bilateral (salpingo-) oophorectomy only or bilateral (salpingo-) oophorectomy with omentectomy. On the other hand, younger patients were more likely to receive bilateral (salpingo-) oophorectomy with hysterectomy or complete surgery. Five-year survival rates of advanced epithelial ovarian cancer patients were much lower than that of the early stage patients, which were all less than 50%. Patients who received complete surgery had a significant improvement in five-year survival than patients who received bilateral (salpingo-) oophorectomy with omentectomy. Similarly, bilateral (salpingo-) oophorectomy with hysterectomy group showed better five-year survival result than the bilateral (salpingo-) oophorectomy only group (not significant, but around the borderline). Therefore, hysterectomy might play an important role in advanced stage epithelial ovarian cancer survival. As stated by Menczer et al. and Behtash et al., advanced stage epithelial ovarian cancer patients had significantly increased the risk of uterine involvement[9, 36]. In Menczer et al. study, 291 out of 263 EOC patients had uterine involvement (78 macroscopic, and 213 microscopic), and more than 95% of them were stage III or higher[9]. Therefore, removing uterus might be an essential part of optimal cytoreduction and thus help improve advanced stage EOC five-year survival. We noticed that patients who received hysterectomy were relatively younger than those who did not, which might also lead to a higher survival rate. We adjusted the effect of age at diagnosis, and the significant improvement in the five-year survival rate persisted. On the other side, omentectomy

did not improve advanced stage EOC five-year survival. Bilateral (salpingo-) oophorectomy with omentectomy group had the lowest five-year survival rate of 41.3%. Complete surgery did not show significantly higher five-year survival rate, so it might not be the best approach for the advanced stage epithelial ovarian cancer patients. Although not statistically significantly different from others, the bilateral (salpingo-) oophorectomy with hysterectomy group had the highest five-year survival rate of 49.9%.

## 5.2 Study Strengths and Limitations

This study has a relatively large sample size. We used the data from the CCR which is a reliable source with a standardized schema. Our study compared the five-year survival rates for four types of surgery plan for both early and advanced stage EOC. However, there are some limitations of our study as well. First, even though the overall study population is large, some early stage surgery groups had a relatively small sample size which may cause variation in survival analysis. Second, although we adjusted the models with the most common characteristics, we could not rule out the effects of other potential factors related to epithelial ovarian cancer survival. Third, all participants in this study received chemotherapy. However, there was no detailed information of the chemotherapy. Therefore, we could not eliminate the effect of different chemotherapy on EOC survival. Furthermore, we did not know the sequence of chemotherapy and surgery. A study showed that patients who received initial surgery followed by adjuvant chemotherapy had a better survival rate than neoadjuvant chemotherapy[37]. Last, the majority of the study was non-Hispanic white female. Therefore, some race/ethnicity groups might have limited population size which would negatively affect the generalizability of the study.

## 5.3 Future Directions

Since the CCR is an ongoing program, more patients can be added to future studies to verify the results. There are limited studies about the effectiveness of hysterectomy and omentectomy on EOC, and the results are controversial. Future studies are needed to test the solo effect of hysterectomy or omentectomy, and the combined effect of the two surgeries.

## 5.4 Conclusions

In conclusion, our study examined the effects of bilateral (salpingo-) oophorectomy, bilateral (salpingo-) oophorectomy with hysterectomy, bilateral (salpingo-) oophorectomy with omentectomy, and complete surgery (bilateral (salpingo-) oophorectomy with hysterectomy and omentectomy) on early and advanced stage EOC five-year survival.

This study suggests that for early stage EOC, neither hysterectomy nor omentectomy could improve five-year survival. Patients who received complete surgery did not have significantly higher five-year survival rate compared to patients who received bilateral (salpingo-) oophorectomy only. Considering the aggressiveness and the effectiveness, complete surgery was not the best approach for early stage EOC patients. For advanced stage EOC patients, bilateral (salpingo-) oophorectomy with hysterectomy revealed a higher but non-significant five-year survival rate compared to bilateral (salpingo-) oophorectomy only. Complete surgery group had a significantly higher five-year survival rate compared to bilateral (salpingo-) oophorectomy with omentectomy. Together these suggested that hysterectomy in addition to bilateral (salpingo-) oophorectomy was essential for improving advanced stage EOC five-year survival. However, omentectomy did not show significant effect on EOC five-year survival. Complete surgery group had a five-year survival rate similar to that of the bilateral (salpingo-) oophorectomy with

hysterectomy group. Again, considering the aggressiveness and the effectiveness, complete surgery was not the best approach for advanced stage EOC patients.

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