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Impact of guideline adherence on patient outcomes in early-stage epithelial ovarian cancer☆

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Abstract

Aim: The aim of this study was to evaluate the effects of adherence to National Comprehensive Cancer Network (NCCN) guidelines on survival outcomes in patients with early-stage epithelial ovarian cancer.

Methods: Our institutional cancer registry data on 266 patients with Stage I epithelial ovarian cancer was reviewed retrospectively and compliance with treatment guidelines for surgery and adjuvant treatment was determined. Patients were categorized according to adherence or non-adherence. The primary endpoints were recurrence-free survival and disease-specific survival. Hazard ratios (HRs) for survival were estimated with a Cox proportional hazards model.

Results: Of the 266 patients, 71 (26.7%) underwent adequate surgical staging in accordance with the guidelines. The guidelines for adjuvant chemotherapy were followed adequately in all 71 patients that were adherent to surgical staging and in 163 of the 195 patients with non-adherence to surgical staging (83.6%). Multivariate analysis, adjusted for prognostic factors, identified higher recurrence-free survival (HR, 0.36; 95% CI, 0.15–0.88) and disease-specific survival (HR, 0.42; 95% CI, 0.16–1.12) among patients whose treatment adhered to both surgical and chemotherapy guidelines, although disease-specific survival was not statistically significant. When excluding clear cell histology from the cohort, the guideline-adherent group had significantly better disease-specific survival than the non-adherent group (HR, 0.13; 95% CI, 0.02–0.94).

Conclusion: The results of this study suggest that adherence to NCCN guidelines may improve survival outcomes in patients with early-stage epithelial ovarian cancer, particularly in cases other than clear cell histology.

Keywords: Ovarian cancer; Guideline adherence; Survival; Surgical staging; Adjuvant chemotherapy

Introduction

Recent studies have shown that adherence to treatment guidelines has survival benefits for cancer patients.[1–3] The National Comprehensive Cancer Network (NCCN) established working, expert consensus, and evidence-based guidelines for organ-specific cancer care in order to provide state-of-the-art treatment information.[4] These guidelines are the most widely used standards for cancer care.

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The current NCCN guidelines for ovarian cancer recommend appropriate surgical staging, followed in most patients by adjuvant chemotherapy. Comprehensive surgical staging should be performed in order to rule out occult metastasis in apparent early-stage disease, as previous reports have shown that around 30% of patients are upstaged after complete staging operation.[5] Approximately 20% of all epithelial ovarian cancer is diagnosed at an early stage and survival rates of 90–100% have been reported for patients who were properly staged and were found to have Stage IA or IB disease.[6] However, a significant proportion of clinicians do not perform complete surgical staging as favorable outcomes are expected in early-stage ovarian cancer.[7,8] Moreover, the unexpected diagnosis of ovarian malignancy is made in between 0% and 19% of cases during a final pathologic examination following a laparoscopic operation.[9] To date, there are few reports that show that compliance with consensus recommendations in early-stage ovarian cancer improves survival outcomes.[7,8]

The aim of this study was to evaluate adherence to treatment guidelines and the impact of adherence to guidelines on survival outcomes in early-stage epithelial ovarian cancer.

Patients and methods

Study population

After receiving institutional review board approval, medical records were reviewed retrospectively for all patients treated surgically for epithelial ovarian cancer between January 1991 and December 2010 at Seoul National University Hospital. Patients were eligible for inclusion if they (1) had International Federation of Gynecology and Obstetrics (FIGO) Stage I epithelial ovarian cancer and (2) had undergone an operation due to an ovarian tumor. A total of 270 women were identified. Four patients were excluded due to a lack of pathologic information and the final study sample comprised 266 patients. Some of the operations (n = 15) were performed by general gynecologists. Otherwise, all surgical procedures (n = 251) were performed by one of six gynecologic oncologists. All cases are part of 324 patients in our previous study.[10] Patient and tumor characteristics, stage, surgical procedure, adjuvant chemotherapy, and date of last contact or date of recurrence/death were collected. Furthermore, information of the cause and date of death was gained from death certificates obtained from the Korea National Statistical Office.

Adherence to guidelines

The definition of adherence or non-adherence to guidelines is based on NCCN recommendations for ovarian cancer. The current NCCN guidelines include both procedures for comprehensive surgical staging and indications for adjuvant chemotherapy.

According to NCCN guidelines, comprehensive surgical staging is recommended for all patients. Adequate surgical staging includes abdominal washing cytology, peritoneal biopsies, bilateral salpingo-oophorectomy, hysterectomy, infracolic omentectomy, pelvic lymph node dissection, and para-aortic lymph node dissection. In selected patients who want to preserve fertility, unilateral salingo-oophorectomy only and inspection of the contralateral ovary and the uterus were accepted. In mucinous histology in particular, appendectomy is recommended during the operation. Surgical staging was classified as adherent if the procedure was performed in accordance with above-mentioned guidelines; otherwise, a patient was classified as non-adherent to surgical guidelines.

Adjuvant chemotherapy is based on the pathologic findings of the surgical specimen. The current NCCN guidelines recommend adjuvant chemotherapy in patients with Stage IA G3, IB G3, or any grade of IC at 3–6 courses of a platinum-based regimen. Patients with Stage IA G1 or IB G1 tumors following surgery were not candidates for adjuvant treatment. For Stage IA G2, IB G2, either observation or adjuvant chemotherapy was allowed. Patients who received adjuvant treatment in accordance with these recommendations were categorized as adherent to chemotherapy.

Adherence to NCCN guidelines in this study is defined as patients who received treatment in accordance with both surgical and chemotherapy guidelines. Patients whose treatment did not follow either the surgical or chemotherapy guidelines were classified as non-adherent.

Statistical analysis

Data from patient demographics and clinical characteristics were summarized using standard descriptive statistics. Survival outcomes were compared for patients treated in accordance with the guidelines and those who were non-adherent. The recurrence-free and disease-specific survival curves were estimated using the Kaplan–Meier method and differences in survival between the groups were compared using the log rank test. Hazards ratios (HRs) for recurrence-free survival and disease-specific survival were estimated with a Cox proportional hazards model. Statistical significance was assumed for $P < 0.05$. All analyses were performed using STATA 11.0 (StataCorp, College Station, TX, USA).

Results

The baseline characteristics are listed in Table 1. The median age is 46.0 years (range: 14–81 years) and the mean follow-up is 8.4 years (range: four months to 22 years). The distribution of tumor grade and histology was significantly different between the guideline adherent and non-adherent groups. Table 2 shows the procedures performed in surgical staging. Para-aortic lymph node

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