GENERAL GYNECOLOGY

What is the optimal treatment for obese patients with advanced ovarian carcinoma?

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OBJECTIVE: The purpose of this study was to compare primary debulking surgery (PDS) vs neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS) among obese patients.

STUDY DESIGN: Medical records of patients with a body mass index (BMI) of ≥30 kg/m^2 with ovarian/fallopian tube/primary peritoneal carcinoma between January 2005 and December 2010 were reviewed. Patients were separated by PDS or NACT-IDS. Preoperative characteristics, surgical procedures, and postoperative and oncologic outcomes were compared.

RESULTS: Of 117 patients, 95 women (81.2%) underwent PDS, and 22 women (18.8%) underwent NACT-IDS. Patients who underwent NACT-IDS were more likely to have stage IV disease (63.6% vs 26.3%; $P = .001$) and a low surgical complexity score (n = 14; 63.6%). There were no other differences between groups with respect to preoperative characteristics or postoperative morbidity. Compared with the NACT-IDS group, the PDS group had an improved progression-free survival (PFS; 15 vs 11 months; $P = .006$) and overall survival (OS; 53 vs 32 months; $P = .036$). Seventy-eight patients (66.7%) had a BMI of 30-34.9 kg/m^2. Within this subset of obese patients, the PDS group had an improved PFS (15 vs 10 months; $P = .011$) and OS (58 vs 32 months; $P = .033$), compared with the NACT-IDS group. Among patients with a BMI of ≥35 kg/m^2, there was no difference in PFS (14 vs 12 months; $P = .316$) or OS (38 vs 32 months; $P = .640$) when the PDS and NACT-IDS groups were compared.

CONCLUSION: Patients with a BMI of 30-34.9 kg/m^2 who undergo PDS have improved oncologic outcomes, compared with those women who undergo NACT-IDS. Patients with a BMI of ≥35 kg/m^2 who undergo PDS have similar oncologic outcomes to those who undergo NACT-IDS. Complication rates were similar at all BMIs, regardless of treatment approach.

Key words: neoadjuvant chemotherapy, obesity, ovarian cancer, primary debulking surgery

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In the final 2 decades of the 20th century, the prevalence of obesity within the United States increased dramatically.[1] The current number of obese persons in the United States is staggering and particularly concerning among women. In 2010, the Centers for Disease Control and Prevention estimated that 40.6 million adult women were obese. Rates of obesity were highest among women >60 years old, because 42.3% of all women in this age group were categorized as obese.[2]

Several studies have shown an increased risk of ovarian cancer among women with a high body mass index (BMI).[3-6] The standard approach to the patient with advanced epithelial ovarian cancer (EOC) remains primary debulking surgery (PDS) followed by platinum-based chemotherapy. Obese patients are more likely than nonobese patients to have medical comorbidities that may increase the risk of postoperative complications.[7,8] Few studies have addressed postoperative complications among obese patients who undergo cytoreductive surgery.[9-12] Bamgbade et al[13] reviewed 94,853 noncardiac procedures and found that, compared with patients with a BMI of <30 kg/m^2, patients with a BMI of ≥30 kg/m^2 were more likely to experience postoperative complications that included wound infection and myocardial infarction. Furthermore, patients with a BMI of ≥35 kg/m^2 had an increased risk of postoperative cardiac arrest and postoperative death.

Neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS) has become a popular alternative to PDS; multiple studies suggest equivalent oncologic outcomes with less surgical morbidity.[14-19] Patients at high risk of surgical morbidity and death may benefit from this approach, but the role of NACT-IDS for obese patients with advanced EOC has yet to be evaluated. The primary objective of the current study was to compare PDS with

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NACT-IDS among obese patients with ovarian/fallopian tube/primary peritoneal carcinoma.

Materials and Methods

After obtaining institutional review board approval, we conducted a retrospective review of all obese patients with advanced stage (FIGO stage IIIC-IV) epithelial ovarian, fallopian tube, or primary peritoneal carcinoma between January 2005 and December 2010 who were treated by PDS or NACT-IDS. *Obesity* was defined as a BMI of $\geq$30 kg/m^2.[20] For patients who were treated by PDS, the preoperative BMI was used. For patients who were treated by NACT-IDS, the BMI at the time of cancer diagnosis was used. Patients were excluded from analysis for the following reasons: never underwent definitive surgical intervention, nonepithelial histologic condition, synchronous or preexisting primary malignancy, or incomplete medical records. All surgical procedures were performed by gynecologic oncology faculty, with intent to achieve optimal cytoreduction ($\leq$1 cm maximal diameter of the largest residual tumor nodule).

Chemotherapy was largely platinum and paclitaxel based and reflected standard protocols used during the study period. For patients who underwent PDS, the final histologic diagnosis was established after pathologic review of the surgical specimen. For patients who underwent NACT-IDS, the final diagnosis was established with a biopsy or cytologic specimen that was consistent with an ovarian, fallopian tube, or primary peritoneal carcinoma. The decision to perform PDS vs NACT-IDS was left at the discretion of the primary gynecologic oncologist. Patients who received neoadjuvant chemotherapy generally received 3-4 cycles of carboplatin (AUC 6) and paclitaxel (175 mg/m^2) every 21 days. Imaging was repeated after 3-4 cycles to evaluate response.

Chemotherapy generally was resumed 3 weeks after surgery with the goal of a total of 6 cycles of chemotherapy. Patients were separated based on PDS or NACT-IDS and compared with respect to preoperative characteristics, surgical procedures performed, and postoperative and oncologic outcomes. To evaluate the impact of the definitive surgical procedure performed, surgical procedures were given a complexity score that reflected the complexity and the number of procedures that were performed as described by Aletti et al.[21] All obese patients (ie, BMI of $\geq$30 kg/m^2) were included in the initial comparison between those who underwent PDS and those who underwent NACT-IDS. We then sought to evaluate PDS vs NACT-IDS among different levels of obesity. The entire obese patient sample was separated into those with a BMI of 30-34.9 kg/m^2 and those with a BMI of $\geq$35 kg/m^2. For these separate obesity groups, those women who underwent PDS and those who underwent NACT-IDS were then compared with respect to the previously mentioned variables. A BMI cut-off of 35 kg/m^2 was used to separate the entire obese patient sample because the World Health Organization recognizes this cut-off as the point at which the risk of comorbidities is severe and the point at which treatment options for obese patients often differ.[20]

Differences in clinical and histopathologic factors between patient groups were examined with the χ^2 and Student *t* test. Progression-free survival (PFS) was calculated from the date of first treatment (surgery or chemotherapy) until the date of first recurrence or last visit. Overall survival (OS) was calculated from the date of first treatment until the date of death, regardless of cause, or the date of last visit if the patient was alive. The Kaplan-Meier method was used to estimate survival curves. Log-rank statistics and Cox proportional hazards regression were used to compare survival data. Associations are shown as hazard ratios (HRs) with 95% confidence intervals (CIs). The SPSS statistical package (version 20.0; SPSS Inc, Chicago, IL) was used for all statistical analyses. A probability value of $<$ .05 was considered to be statistically significant.

Results

Of 117 patient records available for analysis, 95 women (81.2%) underwent PDS and 22 women (18.8%) underwent NACT-IDS. Considering all obese patients, those women who underwent PDS were similar to those who underwent NACT-IDS with respect to BMI, age, CA-125 level, medical comorbidities, previous malignancy, the presence of carcinomatosis, the presence of a pleural effusion (without cytologic evidence), site of origin (ie, ovary, fallopian tube, or peritoneum), histologic type, and histologic grade. The group who underwent NACT-IDS had a greater percentage of patients with stage IV disease (63.6% vs 26.3%; $P = .001$).

Operative procedure characteristics were then compared between the 2 groups. The group who underwent NACT-IDS had a greater percentage of patients with a low surgical complexity score (63.6% vs 34.7%; $P = .016$). The rates of optimal cytoreduction and cytoreduction to no gross residual disease (NED) were similar between groups (Table 1). We then compared groups with respect to postoperative morbidity and mortality rates. There were no differences between the PDS and NACT-IDS group with respect to hospital length of stay, number of transfused units of blood, or postoperative complications (Table 2).

Of the 95 patients in the PDS group, there were 76 recurrences (80%); of the 22 patients in the NACT-IDS group, there were 21 recurrences (95.5%). Compared with those women who underwent NACT-IDS, the group who underwent PDS had a greater median PFS (15 vs 11 months; $P = .006$). On univariate analysis, factors associated with recurrence included the presence of carcinomatosis (HR, 2.55; 95% CI, 1.55–4.20), the presence of a pleural effusion (HR, 1.79; 95% CI, 1.13–2.83), NACT-IDS (HR, 1.94; 95% CI, 1.18–3.17), stage IV disease (HR, 1.54;95% CI, 1.02–2.34), optimal cytoreduction (HR, 0.53; 95% CI, 0.30–0.93), and cytoreduction to NED (HR, 0.41; 95% CI, 0.22–0.77). On multivariate analysis, the presence of carcinomatosis (HR, 1.87; 95% CI, 0.06–3.30) and the use of NACT-IDS (HR, 2.31; 95% CI, 1.29–4.15) were associated independently with an increased risk of recurrence.

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