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Does neoadjuvant chemotherapy decrease the risk of hospital readmission following debulking surgery?

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HIGHLIGHTS

- Elderly patients undergoing either PDS or NACT-IDS have similar oncologic outcomes.
- The risk of readmission within 30 days of surgery is significantly greater among patients undergoing PDS.

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ABSTRACT

Objective. To compare primary debulking surgery (PDS) vs. neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS) among elderly patients with ovarian/fallopian tube/primary peritoneal carcinoma.

Methods. Medical records of patients ≥70 years old with epithelial ovarian/fallopian tube/primary peritoneal carcinoma between January 2000 and December 2010 were reviewed. Patients were separated by PDS or NACT-IDS. Preoperative characteristics, surgical procedures and postoperative and oncologic outcomes were compared. Surgical procedures were given a complexity score based on a previously published method.

Results. Of 165 patients, 125 (75.8%) underwent PDS and 40 (24.2%) underwent NACT-IDS. Patients undergoing NACT-IDS were more likely to have a pleural effusion (without cytology) and stage 4 disease. Median CA-125 at diagnosis was greater for those undergoing NACT-IDS. The NACT-IDS group was associated with less intraoperative blood loss (250 vs. 400 mL, $p=0.001$), a greater chance of achieving no residual disease (40% vs. 16%, $p=0.005$) and a shorter hospital length of stay (LOS) (5 vs. 7 days, $p<0.001$). PFS (17 vs. 15 months, $p=0.708$) and OS (29 vs. 33 months, $p=0.827$) were similar between the two groups. Readmission rates within 30 days of surgery were greater in those undergoing PDS (17.6% vs. 2.5%, $p=0.016$). After readmission, the median hospital LOS was 6 days (range: 1–41).

Conclusions. Elderly patients undergoing PDS have similar oncologic outcomes when compared to patients undergoing NACT-IDS. The risk of readmission within 30 days of surgery is significantly greater among patients undergoing PDS.

Introduction

In 2012, the American Cancer Society estimated that about 22,000 women would be newly diagnosed with ovarian cancer and that about 15,000 women would die of their disease [1]. With a peak incidence in the seventh decade of life and close to 50% of newly diagnosed women at least 65 years of age, ovarian cancer is primarily a disease of the elderly woman [2,3].

Previous studies have shown that when compared to younger women, those older than 65 years of age have significantly worse rates of survival. While age alone is a prognostic factor, numerous other factors contribute to poor survival including biological disease aggressiveness and medical comorbidities [3–5]. The ideal treatment approach for older women remains poorly defined and variations in patient care may also contribute to the discrepancy in survival rates when compared to younger women. Specifically, elderly women with ovarian cancer are less likely to receive care with a gynecologic oncologist, undergo aggressive cytoreductive surgery and are less likely to receive platinum-based chemotherapy and/or clinical trial participation [2,4,6–10].

While the standard approach to the patient with advanced epithelial ovarian cancer (EOC) remains primary debulking surgery (PDS) followed

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by platinum-based chemotherapy, neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS) is a treatment approach gaining increasing popularity [11,12]. Several studies have suggested that NACT-IDS does not impair overall survival (OS) while at the same time increases the likelihood of optimal debulking with less surgical morbidity, when compared to PDS [13,14]. With this in mind, NACT-IDS appears to be an attractive alternative to PDS for a population of patients often associated with frailty and complex medical histories. As previously mentioned, a paucity of data exists evaluating elderly women with EOC and so the ideal treatment approach remains a topic of debate. The objective of the current study was to compare survival outcomes of elderly patients newly diagnosed with ovarian, fallopian tube or primary peritoneal carcinoma managed with either PDS or NACT-IDS. In addition, we sought to compare elderly patients managed with PDS or NACT-IDS with respect to: preoperative characteristics, surgical procedures performed and postoperative complications in an attempt to identify predictive factors for perioperative morbidity.

Materials and methods

After obtaining institutional review board (IRB) approval, we conducted a retrospective chart review of all patients ≥70 years old diagnosed with advanced stage (FIGO IIIC-IV) epithelial ovarian, fallopian tube or primary peritoneal carcinoma between January 2000 and December 2010 undergoing either PDS or NACT-IDS. Patients were excluded from the final analysis for the following reasons: never underwent definitive surgical intervention, non-epithelial histology, synchronous or pre-existing primary malignancy or incomplete medical records. The cutoff of ≥70 years old was used to define "elderly" patients based on previously published studies [15]. All surgical procedures were performed by gynecologic oncology faculty, with intent to achieve optimal cytoreduction. Optimal cytoreduction was defined as less than or equal to 1 cm maximal diameter of the largest residual tumor nodule at the completion of the primary operation. Chemotherapy was largely platinum and paclitaxel based and reflected standard protocols used during the study period. For patients undergoing PDS, the final histologic diagnosis was established after pathologic review of the surgical specimen. For patients undergoing NACT-IDS, the final diagnosis was established with a biopsy or cytology specimen consistent with an ovarian, fallopian tube or primary peritoneal carcinoma. The decision to perform PDS vs. NACT-IDS and the initial chemotherapy regimen was determined after a review of the patient's overall performance status, medical comorbidities and likelihood of optimal cytoreduction. Patients receiving 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. All patients underwent exploration to further evaluate respectability. Chemotherapy was generally resumed 3 weeks after surgery with the goal of a total of 6 cycles of chemotherapy. Preoperative chemotherapy agents were generally resumed. However, in the setting of a poor response or progression during chemotherapy, agents were generally altered. 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 which reflected the complexity and the number of procedures performed as described by Aletti et al. [16].

Differences in clinical and histopathologic factors between patient groups were examined with the χ^2 and Student's *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. 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 (HR) with 95% confidence intervals. The SPSS version 20.0 statistical package was used for all statistical analyses. A p-value of less than 0.05 was considered to be statistically significant.

Results

A total of 165 patients were available for analysis. 125 (75.8%) underwent PDS and 40 (24.2%) underwent NACT-IDS. The median patient age for all patients analyzed was 75 years old. There was no difference in median age when comparing those undergoing NACT-IDS and those undergoing PDS (74 vs. 75 years old, p = 0.102). A further comparison of preoperative and pathologic characteristics between the PDS and NACT-IDS groups is displayed in Table 1. Notably, when compared to the PDS group, patients undergoing NACT-IDS were significantly more likely to have a pleural effusion (without cytologic confirmation of malignancy) (27.5% vs. 10.4%, p = 0.008) and stage IV disease (42.5% vs. 13.6%, p < 0.0001). There was no significant difference between groups with respect to carcinomatosis or medical comorbidities, with the exception of asthma which was more common in those receiving NACT-IDS (22.5% vs. 3.2%, p < 0.0001). The group undergoing NACT-IDS had a significantly higher median CA-125 value at diagnosis, when compared to the group undergoing PDS (1210 U/mL vs. 449 U/mL, p = 0.021).

Operative procedure characteristics were then compared between the two groups and are shown in Table 2. While the surgical complexity scores did not differ significantly between patients undergoing PDS and NACT-IDS, the PDS group was associated with greater intraoperative blood loss (median: 400 mL vs. 250 mL, p = 0.001).

Table 1
Comparison of patient and pathologic characteristics by treatment approach.

Characteristic	Primary debulking surgery (n = 125)	Neoadjuvant chemotherapy (n = 40)	p-Value
Age (years)[a]	75 (70–95)	74 (70–84)	0.102
CA-125 at diagnosis (U/mL)[a]	449 (12–17,700)	1210 (13–14,258)	0.021
HTN	74 (59.2%)	23 (57.5%)	0.849
CAD	15 (12%)	7 (17.5%)	0.373
DM	18 (14.4%)	4 (10%)	0.476
Obesity	22 (17.6%)	5 (12.5%)	0.448
Asthma	4 (3.2%)	9 (22.5%)	<0.0001
COPD	9 (7.2%)	4 (10%)	0.567
Prior malignancy	18 (14.4%)	8 (20%)	0.397
Carcinomatosis	104 (83.2%)	38 (95%)	0.61
Pleural effusion (without cytology)	13 (10.4%)	11 (27.5%)	0.008
Site of origin			0.095
Ovary	98 (78.4%)	36 (90%)	
Fallopian tube	13 (10.4%)	0 (0%)	
Peritoneum	14 (11.2%)	4 (10%)	
Histologic type			0.216
Serous	104 (83.2%)	35 (87.5%)	
Mucinous	4 (3.2%)	0 (0%)	
Clear cell	1 (0.8%)	0 (0%)	
Endometrioid	7 (5.6%)	1 (2.5%)	
Undifferentiated	4 (3.2%)	3 (7.5%)	
Mixed	5 (4%)	0 (0%)	
Unknown	0 (0%)	1 (2.5%)	
Grade			0.017
Well-differentiated	7 (5.6%)	0 (0%)	
Moderately-differentiated	14 (11.2%)	0 (0%)	
Poorly-differentiated	102 (81.6%)	38 (95%)	
Unknown	1 (0.8%)	2 (5%)	
FIGO stage[b]			<0.0001
IIIC	108 (86.4%)	23 (57.5%)	
IV	17 (13.6%)	17 (42.5%)	

[a] Values displayed represent median (range).
[b] Patients without cytologic confirmation of a malignant pleural effusion were not grouped as stage IV.