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Intensive care admissions among ovarian cancer patients treated with primary debulking surgery and neoadjuvant chemotherapy-interval debulking surgery

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HIGHLIGHTS

- Intensive care unit (ICU) admissions are more common in ovarian cancer patients treated with primary debulking (PDS).
- This was true though patients treated with neoadjuvant chemotherapy (NACT) were older and had more advanced disease.
- NACT patients admitted to the ICU had comparable surgical complexity at time of cytoreduction as PDS ICU admitted patients.
- Indications of ICU admission were not different between patients undergoing PDS vs NACT.

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ABSTRACT

Objective. Admissions to intensive care units (ICU) are costly, but are necessary for some patients undergoing radical cancer surgery. When compared to primary debulking surgery (PDS), neoadjuvant chemotherapy (NACT) with interval debulking surgery, is associated with less peri-operative morbidity. In this study, we compare rates, indications and lengths of ICU stays among ovarian cancer patients admitted to the ICU within 30 days of cytoreduction, either primary or interval.

Methods. A retrospective chart review was performed of patients with stage III-IV ovarian cancer who underwent surgical cytoreduction at two large academic medical centers between 2010 and 2014. Chi square tests, Student *t*-tests, and Mann-*U* Whitney tests were used.

Results. A total of 635 patients were included in the study. There were 43 ICU admissions, 7% of patients. Compared to NACT, a higher percentage of PDS patients required ICU admission, 9.4% vs 3.9% of patients ($P = 0.004$). ICU admission indications did not vary between PDS and NACT patients. NACT patients admitted to the ICU had comparable mean surgical complexity scores to those PDS patients admitted to the ICU, 6.2 (95%CI 5.3–7.1) vs 4.5 (95%CI 3.1–6.0) ($P = 0.006$). Length of ICU admission did not vary between groups, PDS 2.7 days (95%CI 2.3–3.2) vs 3.5 days (95%CI 1.5–5.6) for NACT ($P = 0.936$).

Conclusions. The rate of ICU admissions among patients undergoing PDS is higher than for NACT. Among patients admitted to the ICU, indications for admission, length of stay and surgical complexity were similar between patients treated with NACT and PDS.

1. Introduction

Admission to an intensive care unit (ICU) represents a significant cost to the health care system [1]. It has been estimated to account for over half a percent of the United States Gross Domestic Product (GDP) [1]. Given the lack of screening for detection of early-stage ovarian cancer, an estimated 85% of patients with epithelial ovarian cancer present with advanced-stage (III/IV) disease and require radical debulking surgery, either upfront or as an interval strategy, which often necessitates ICU-level of care. Post-operative ICU admission rates after ovarian cancer debulking surgery have been reported to be as high as 30% [2]. Predictors of extended ICU stay in these patients include older age, more medical comorbidities and more extensive surgical debulking [3].

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Since the publication of two phase III randomized clinical trials, Kehoe et al. and Vergote et al., showing equivalent survival between ovarian cancer patients treated with primary debulking surgery (PDS) and neoadjuvant chemotherapy with interval debulking surgery (NACT), the use of NACT has increased [4–6]. NACT has become a preferred paradigm for the management of patients with unresectable disease upfront or those too medically infirmed to undergo PDS. This is despite the relatively low rates of resection to no residual disease (R0) and lower than previously reported survival, in these trials [5–6]. Though poor candidates for upfront surgery, were historically offered NACT, the before mentioned non-inferiority trials, have likely resulted in a lower the threshold to offer patients NACT. Several studies have reported fewer post-operative complications and lower 30-day mortality among patients treated with NACT vs PDS [5–6].

With the recent shift in treatment of older and more medically complex women with NACT, there have been no accompanying data on how ICU utilization has been affected. In this study, we compare rates, indications and lengths of ICU stays among ovarian cancer patients admitted to the ICU within 30 days of cytoreduction, either primary or interval.

2. Methods

We identified all newly diagnosed stage III-IV epithelial ovarian, fallopian tube and primary peritoneal cancer patients who underwent surgical cytoreduction, at two large academic medical centers between 2010 and 2014. A joint institution Institutional Review Board (IRB) approved the retrospective chart review and analysis. Patients were identified using tumor registries and tumor board records. Patients with early stage tumors, germ cell tumors and borderline tumors were not included in the analysis. Patients who were treated exclusively with chemotherapy were excluded from the study, as were patients who underwent debulking surgery at an outside facility.

Patients were defined as having had primary debulking surgery if surgery was the first treatment modality the patient underwent, and an attempt at debulking was made at the time of surgery. Patients who received only surgery, and no adjuvant chemotherapy were considered part of the PDS group. The NACT group was defined by any chemotherapy prior to attempt at surgical debulking. In most cases, the planned course was for a debulking procedure following 3 cycles of NACT.

The Charlson Comorbidity Index was used to evaluate preoperative comorbid conditions at the time of diagnosis. The index includes predicts 10-year mortality, based on history of myocardial infarction, congestive heart failure, renal disease, diabetes, chronic obstructive pulmonary disease, liver disease, dementia, peripheral vascular disease, peptic ulcer disease, hemiplegia and malignancy. All patients in the study, by definition, had metastatic cancer, earning a Charlson Comorbidity score of 6. For this analysis, their scores were calculated excluding their cancer diagnosis, such that the lowest possible score was zero [7]. Additionally, no condition included in the Comorbidity index should have been significantly improved by use of chemotherapy, thus scores were not recalculated after completion of NACT.

Surgical morbidity was characterized by the surgical procedures performed at the time of cytoreduction, including bowel resection, ostomy creation, splenectomy, liver resection and procedures on the diaphragm. All procedures performed were incorporated into a surgical complexity score, to compare the extent of surgical debulking [8]. One point was assigned for hysterectomy/bilateral salpingo-oophorectomy, omentectomy, pelvic lymph node dissection, paraaortic lymph node dissection and small bowel resection. Two points were assigned for large bowel resection, diaphragm stripping/resection, splenectomy and liver resection. Three points were assigned for a rectosigmoid resection with anastomosis. Post-operative morbidity was defined by estimated blood loss (EBL) >2 l, intensive care unit (ICU) admission, need for re-operation, hospital length of stay (LOS), and readmission within 30-days.

Descriptive statistics were defined with means and medians. Chi square tests, Student *t*-tests, and Mann-*U* Whitney tests were used to evaluate categorical and continuous variables. All analysis was performed in SPSS.

3. Results

A total of 635 patients met inclusion criteria for the study. There were 43 ICU admissions, just 7% of patients who underwent surgical debulking during this time period. The median age was 64 (range 27–93) and median BMI 25.5 (range 16.1–72.1). Of the included patients, 459 (72%) had stage III disease and 176 (28%) had stage IV disease. Age, race, BMI, diagnosis CA 125 (including CA 125 prior to initiation of chemotherapy for NACT patients), comorbidity index and stage did not vary significantly between patients who were and were not admitted to an ICU post-operatively (Table 1). Those undergoing NACT were older, 64.1 years (range 34–89), than those undergoing PDS, 62 (range 27–93) ($P = 0.008$) and were more likely to have stage IV disease; 42% of NACT patients vs 14% PDS patients ($P = 0.000$). Comorbidity index did not vary significantly between the two surgical groups. Rates of NACT rose overtime during the study period ($P = 0.001$) (Fig. 1). Among the NACT patients, <1% received <3 cycles of preoperative chemotherapy, 55% received three cycles of preoperative chemotherapy, 28% received four cycles of preoperative chemotherapy and the remainder received >4 cycles of preoperative chemotherapy. Three patients treated with neoadjuvant chemotherapy underwent a laparoscopic debulking procedure, with the rest done via laparotomy.

The most common indications for ICU admission were hemodynamic monitoring/pharmacologic blood pressure support (84.1%), respiratory failure/inability to extubate (22.7%), bacteremia/sepsis (18.2%), anastomotic leak (9.1%), cardiac indication (4.6%), neurologic indication (4.5%) and open abdomen (4.5%). Fourteen patients had more than one indication for ICU admission. Patients requiring ICU admission had higher estimated blood loss; 1630 ml (95%CI 1181–2147) vs 503 ml (95%CI 453–540), ($P < 0.001$). ICU admission indications did not vary between PDS and NACT patients (Fig. 2). Patients admitted to a ICU had significantly higher pre-operative CA −125 levels; 4125 U/ml (95%CI 702–11,135) vs 545 U/ml (95%CI 435–678), ($P < 0.001$). Most patients were admitted to the ICU during the initial hospitalization,

Table 1
Patient characteristics.

	ICU admitted		Non-ICU admitted		P value
	Mean	Range	Mean	Range	
Age	64	39–79	63	26–93	0.547
BMI	26.8	19.0–45.9	26.5	16.1–72.1	0.565
Dx CA 125	6080	4–37,600	1445	22–103,525	0.267
	Number	%	Number	%	P value
Race					0.232
White	26	61%	470	80%	
Black	2	5%	14	2%	
Hispanic	0	0%	8	1%	
Asian	3	7%	18	3%	
Other/Pt declined	8	27%	56	14%	
Stage					0.283
3	430	73%	29	67%	
4	162	27%	14	33%	
Histology					0.952
Serous	387	65%	27	63%	
Other	205	35%	16	26%	
Comorbidity index					
0	62	10%	2	5%	0.204
1	128	22%	9	21%	
2	166	28%	15	35%	
3	135	23%	7	16%	
4 or greater	101	17%	10	23%	
Neoadjuvant chemotherapy	12	28%	294	50%	0.000

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