



# Impact of hospital surgical volume on complete gross resection (CGR) rates following primary debulking surgery for advanced stage epithelial ovarian carcinoma

Dimitrios Nasioudis<sup>a,\*</sup>, Ryan Kahn<sup>b</sup>, Eloise Chapman-Davis<sup>b</sup>, Melissa K. Frey<sup>b</sup>, Thomas A. Caputo<sup>b</sup>, Steven S. Witkin<sup>b</sup>, Kevin Holcomb<sup>b</sup>

<sup>a</sup> Division of Gynecologic Oncology, University of Pennsylvania Health System, Philadelphia, PA, USA

<sup>b</sup> Division of Gynecologic Oncology, Weill Cornell Medicine, NY, New York, USA

## HIGHLIGHTS

- Among 8894 patients with bulky stage III disease undergoing PDS rate of CGR was 42.2%.
- Patients receiving PDS for advanced stage EOC in high volume centers had a higher likelihood of CGR.
- Centralization of ovarian cancer surgery may be associated with better outcomes.

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## ABSTRACT

**Background.** To investigate the impact of hospital surgical volume on the rate of complete gross resection for patients with advanced stage epithelial ovarian carcinoma undergoing primary debulking surgery.

**Methods.** The National Cancer Data Base was used to identify patients undergoing between 2010 and 2014 for an advanced stage (III-IV) epithelial ovarian cancer. For analyses purposes facility surgical volume was divided into tertiles (high, intermediate and low). Patients with bulky stage III disease who underwent primary debulking surgery with known residual disease status were selected for further analysis.

**Results.** A total of 8894 patients with macroscopic peritoneal disease were included. Rates of complete gross resection for patients managed in low, intermediate and high-volume centers were 41.0%, 41.6% and 43.3% respectively ( $p = 0.20$ ). After controlling for year of diagnosis, age, insurance status, presence of co-morbidities, histology, size of peritoneal implants, stage, and complexity of surgery, patients undergoing primary debulking surgery at low (OR: 0.85, 95% CI: 0.74, 0.97,  $p = 0.013$ ) and intermediate (OR: 0.90, 95% CI: 0.82, 0.99,  $p = 0.043$ ) volume centers had a lower likelihood of achieving complete gross resection compared to those managed in high volume centers.

**Conclusions.** After controlling for multiple potential confounders, patients receiving surgery in high volume centers had a higher likelihood of complete gross resection following primary debulking surgery for advanced-stage epithelial ovarian cancer.

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## 1. Introduction

An estimated 22,530 new cases of ovarian cancer will be diagnosed in the United States in 2019 [1]. Ovarian cancer accounts for 5% of overall cancer deaths and causes more deaths in the United States than all other gynecologic malignancies combined [1,2]. Roughly 4 out of

every 5 patients with epithelial ovarian cancer present with advanced-stage disease at the time of diagnosis [1].

Ovarian cancer debulking, or cytoreduction surgery, refers to an aggressive surgical attempt to achieve minimal residual disease. Gynecologic surgeon Joe Vincent Meigs introduced the concept of ovarian cancer debulking in 1934, while C.T. Griffiths first correlated size of residual disease with survival [3,4]. Nearly 85 years later, the combination of surgical cytoreduction and systemic chemotherapy remains the preferred initial management for patients with advanced epithelial ovarian cancer. The Gynecologic Oncology Group defines optimal cytoreduction as residual disease that is  $\leq 1$  cm in maximum tumor diameter, complete

\* Corresponding author at: Division of Gynecologic Oncology, Hospital of the University of Pennsylvania, 3400 Spruce Street, 1 West Gates, Philadelphia, PA 19104, USA.  
E-mail address: [dimitrios.nasioudis@uphs.upenn.edu](mailto:dimitrios.nasioudis@uphs.upenn.edu) (D. Nasioudis).

cytoreduction as no grossly visible disease, and suboptimal cytoreduction as residual tumor nodules >1 cm in diameter [5]. The greatest survival benefit, however, is seen in patients who achieve removal of all macroscopic disease [6–8].

The impact of hospital surgical volume on the survival of patients with epithelial ovarian cancer remains a subject of debate. Several studies have shown that patients managed at facilities with high surgical volume have improved overall survival, supporting the centralization of care in high volume centers [9,10]. However, others authors have presented contradictory evidence, demonstrating no significant difference in ovarian cancer outcomes based on hospital volume [11–13]. Additionally, there is sparse evidence regarding an association between surgical caseload and the rates of complete, optimal, and suboptimal debulking. The aim of the present study was to investigate the impact of hospital surgical volume on the rates of complete gross cytoreduction following primary debulking surgery of advanced epithelial ovarian cancer using a large hospital-based database.

## 2. Methods

The National Cancer Data Base was accessed and patients diagnosed between 2010 and 2014 with a microscopically confirmed advanced stage (III–IV) malignant ovarian tumor were identified. Based on International Classification of Diseases in Oncology histology codes (as grouped by the International Agency for Research on Cancer) those with endometrioid, mucinous, clear cell or serous carcinoma who underwent surgical treatment at the reporting facility were selected for further analysis. This cohort was used to calculate the average annual surgical volume. More specifically, average annual surgical volume for each reporting facility was calculated by dividing the number of patients who met the initial inclusion criteria managed at each reporting facility by the number of years with reported data. Hospital volume was divided into tertiles (high, intermediate, low volume) similar to prior analyses investigating the impact of facility volume on oncologic outcomes in other surgical disciplines, to provide a fair comparison between cancer centers, reflecting oncologic care in the U.S [14,15].

The National Cancer Database, established jointly by the American Cancer Society and Commission on Cancer of the American College of Surgeons, is a hospital-based database capturing approximately 70% of all malignancies diagnosed in the United States. Patient data are prospectively collected from participating commission-accredited cancer programs and are frequently audited to ensure high-quality. All data are de-identified and available for research purposes. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytical or statistical methodology employed, or the conclusions drawn from these data. The present study was deemed exempt from Institutional Board Review.

Based on the extent of disease variable of the collaborative staging schema patients with bulky stage III disease (T3b or T3c) were selected. Patients with stage IIIA disease or microscopic peritoneal metastases were excluded. Patients who received neoadjuvant chemotherapy or more than one surgical debulking surgeries were excluded. Based on information available in the collaborative staging schema, patients who had complete gross resection (CGR) following primary debulking surgery were identified. Since 2010, the NCDB has required registrars to collect information on the residual tumor status as described by the surgeon in the operative report. Previous studies have used data from NCDB to report on residual disease status and survival in ovarian cancer patients [16,17]. The extent of surgery was assessed from site-specific surgery codes and procedures with codes corresponding to “debulking/cytoreductive surgery” were defined as complex surgery while those with codes “hysterectomy, omentectomy, bilateral salpingo-oophorectomy” were defined as low complexity. Presence of co-morbidities was assessed from the Charlson-Deyo Comorbidity index and was categorized as absent (score 0) or present (score  $\geq 1$ ).

Demographic and clinico-pathological characteristics of the patient population were extracted from the de-identified National Cancer Database dataset and compared with the Mann-Whitney U and chi-square tests. Multivariable analysis was performed with binary logistic regression to evaluate the impact of hospital volume on the odds of achieving complete gross resection. All statistical analysis was performed with the Statistical Package for the Social Sciences v.24 statistical package (IBM Corp. Armonk, NY) and the alpha level of statistical significance was set at 0.05.

## 3. Results

A total of 26,022 patients with stage III/IV serous, endometrioid, mucinous or clear cell ovarian carcinoma who underwent surgery at the reporting facility were identified. This cohort was used to calculate average annual surgical volume for each reporting facility. 19.3% of patients underwent surgery in low volume centers ( $\leq 6.8$  cases per year) while 43% and 37.7% in intermediate (6.81–17.2 cases per year) and high ( $>17.2$  cases per year) surgical volume centers, respectively.

A total of 8894 patients with bulky stage III disease who underwent primary debulking surgery and had known residual disease status comprised the analysis cohort. The rate of complete gross resection (GCR) was 42.2% (3751 patients). Patients managed in low volume centers were less likely (68%) to undergo surgical procedures coded as “debulking/cytoreductive surgery” compared to those managed in intermediate (72.3%) and high (75.6%) centers,  $p < 0.001$ . Table 1 presents the demographic and clinico-pathological characteristics of the present cohort stratified by residual disease status. Higher rates of CGR were observed among patients managed in facilities at the Midwest, those with private insurance, as well as for patients diagnosed in 2013 and 2014. Presence of medical comorbidities, patient age and race were not associated with CGR.

Based on univariate analysis rates of CGR for patients managed in low, intermediate and high surgical volume centers were 41.0%, 41.6% and 43.3% respectively ( $p = 0.20$ ). However, by binary logistic regression after controlling for year of diagnosis, facility location, patient age, insurance status, presence of co-morbidities, tumor histology, size of peritoneal implants ( $\leq 2$  cm vs  $>2$  cm), disease stage, and complexity of surgical procedure, patients undergoing primary debulking surgery in low (OR: 0.85, 95% CI: 0.74, 0.97,  $p = 0.013$ ) and intermediate (OR: 0.90, 95% CI: 0.82, 0.99,  $p = 0.043$ ) volume centers had lower likelihood of achieving CGR compared to those managed in high volume centers (Table 2). For patients with gross residual disease and known size of residual disease ( $n = 3985$ ), the rate of sub-optimal debulking (defined as macroscopic residual disease  $> 1$  cm) for patients managed in low, intermediate and high volume surgical centers was 24.6%, 24.8% and 23.9% respectively, ( $p = 0.80$ ). A total of 1158 patients were coded as “macroscopic residual tumor, size not stated”. While these patients did not have a CGR we could not assess whether they underwent optimal or suboptimal debulking.

Ninety-day mortality was higher in low volume hospitals (5.1%) compared to intermediate (3.3%) and high (3.4%) volume facilities ( $p = 0.013$ ) while thirty-day mortality was comparable (1.7%, 1.4% and 1.4%, respectively  $p = 0.64$ ). Similarly, the rate of unplanned readmission within thirty days from discharge was comparable between low (7.6%), intermediate (7.1%) and high (6.8%) volume centers.

## 4. Discussion

In this large cohort of patients with advanced stage ovarian cancer who underwent primary debulking surgery, higher hospital surgical volume was associated with a greater likelihood of achieving CGR. Main strength of the present study was the large number of patients and participating institutions (both academic and non-academic centers), since the NCDB covers 70% of all newly diagnosed cancer cases in the U.S.

**Table 1**  
Clinico-pathological characteristics of patients with advanced stage epithelial ovarian cancer undergoing primary debulking surgery stratified by residual disease status.

	R0	Gross residual disease	p value
Hospital volume			0.20
High	1477 (39.4%)	1932 (37.6%)	
Intermediate	1651 (44%)	2314 (45%)	
Low	623 (16.6%)	897 (17.4%)	
Facility location <sup>a</sup>			0.018
Midwest	975 (27.1%)	1230 (24.7%)	
Northeast	683 (19%)	917 (18.4%)	
South	1300 (36%)	1844 (37%)	
West	643 (17.9%)	992 (19.9%)	
Year of diagnosis			0.006
2010	689 (18.4%)	983 (19.1%)	
2011	751 (20%)	1115 (21.7%)	
2012	738 (19.7%)	1074 (20.9%)	
2013	795 (21.2%)	1047 (20.4%)	
2014	778 (20.7%)	924 (18%)	
Age			<0.001
<65 y	2301 (61.3%)	2941 (57.2%)	
≥65 y	1450 (38.7%)	2202 (42.8%)	
Race <sup>a</sup>			0.43
White	3282 (88.1%)	4535 (88.7%)	
Non-white	442 (11.9%)	579 (11.3%)	
Comorbidities			0.13
No	3077 (82%)	4153 (80.8%)	
Yes	674 (18%)	990 (19.2%)	
Insurance <sup>a</sup>			<0.001
Private	1993 (53.9%)	2484 (48.7%)	
Government	1567 (42.4%)	2421 (47.5%)	
Uninsured	136 (3.7%)	194 (3.8%)	
Histology			<0.001
Serous	3302 (88%)	4704 (91.5%)	
Non-serous	449 (12%)	439 (8.5%)	
Stage			<0.001
III	3303 (88.1%)	4081 (79.4%)	
IV	448 (11.9%)	1062 (20.6%)	
Extent of peritoneal disease			<0.001
T3B	705 (18.8%)	517 (10.1%)	
T3C	3046 (81.2%)	4626 (89.9%)	
Complex surgery <sup>a</sup>			<0.001
No	1371 (36.6%)	1039 (20.3%)	
Yes	2376 (63.4%)	4089 (79.7%)	
Chemotherapy			0.001
Yes	3361 (89.6%)	4717 (91.7%)	
No	390 (10.4%)	426 (8.3%)	

<sup>a</sup> Missing values: insurance (99 patient), race (56 patients), complex surgery (19 patients), facility location (310 patients).

These findings are consistent with those of Vernooij et al. [18], who demonstrated higher odds of optimal debulking for stage III ovarian cancer patients treated in specialized hospitals and high-volume centers (OR 2.8) [18]. In another study, conducted in Austria, patients undergoing surgery at large volume departments (defined as ≥24 patients per year) had a slightly higher rate of complete cytoreduction (46% vs 43%,  $p < 0.01$ ) [19]. Olaitan et al. [20], also concluded that patients treated in hospitals managing <10 cases of ovarian cancer per year were less likely to achieve optimally cytoreduction (OR: 1.92,  $p = 0.02$ ) [20]. Similarly in an analysis of the Danish Gynecological Cancer Database patient with bulky disease managed at a tertiary (high volume) center had a higher likelihood of complete cytoreduction (HR: 2.46) [21]. Kumpulainen et al. [22] also found that hospital operative volume was associated with residual disease; as volume increased by 10 patients per year, the odds for complete gross resection was 1.2 [22].

The higher optimal debulking rates observed in high volume centers may be attributed to a more efficient preoperative selection of patients who can benefit from primary debulking surgery. In an effort to quantify the extent of disease and optimally triage patients both clinico-radiological and laparoscopic scoring systems have been proposed [23–25]. Further research is necessary to externally validate these systems in order to utilize in ovarian cancer treatment centers. In addition, in our cohort lower volume centers were less likely to perform complex

**Table 2**  
Independent predictors of complete gross resection (CGR) following primary debulking surgery for patients with advanced stage epithelial ovarian cancer.

	OR (95% CI)	p value
Hospital volume		0.024
High	Ref	
Intermediate	0.90 (0.82, 0.99)	
Low	0.85 (0.74, 0.97)	
Year of diagnosis		0.002
2010	Ref	
2011	0.99 (0.86, 1.14)	
2012	1.01 (0.88, 1.17)	
2013	1.15 (1.00, 1.32)	
2014	1.26 (1.09, 1.45)	
Age		0.69
<65 y	Ref	
≥65 y	0.98 (0.86, 1.10)	
Facility location		0.19
Midwest	Ref	
Northeast	1.00 (0.87, 1.14)	
South	0.95 (0.85, 1.07)	
West	0.87 (0.76, 1.00)	
Comorbidities		0.21
No	Ref	
Yes	0.93 (0.83, 1.04)	
Insurance		0.009
Private	Ref	
Government	0.84 (0.74, 0.95)	
Uninsured	0.83 (0.65, 1.06)	
Histology		0.001
Serous	Ref	
Non-serous	1.30 (1.12, 1.51)	
Stage		<0.001
III	Ref	
IV	0.57 (0.51, 0.65)	
Extent of peritoneal disease		<0.001
T3B	Ref	
T3C	0.56 (0.50, 0.65)	
Complex surgery		<0.001
No	Ref	
Yes	0.48 (0.44, 0.55)	

surgical procedures. Similar to our results, in an analysis of the Multicentre Italian Trials in Ovarian Cancer (MITO) database patients treated in tertiary referral centers were more likely to achieve complete cytoreduction (60% vs 24.6%,  $p < 0.001$ ), while they also underwent more complex procedures (81.4% vs 50.8%,  $p < 0.001$ ) compared to those managed in non-oncologic referral gynecologic surgery centers [26]. Marth et al. [19] also reported higher rates of bowel surgery among patients treated in high volume departments [19]. In addition, it should be noted that patients in lower volume centers may not have been managed by a gynecologic oncologist. Subspecialty of surgeon has been previously correlated with surgical outcomes among patients with ovarian cancer [20,27,28].

Complete cytoreduction has been strongly correlated with survival for ovarian cancer patients with advanced stage disease [8,29]. The success of complete cytoreduction surgery depends on various factors, including extent of tumor bulk, bowel involvement, patient selection, and presence of ascites [30–32]. While the positive impact of complete cytoreduction on overall survival in advanced epithelial ovarian cancer is well established, it remains controversial whether the improved outcomes are related to the surgeon's technical skill, biological characteristics of the cancer, or combination of the two. A retrospective study by Aletti et al. comparing surgeons who perform radical procedures in more than 50% of their cases versus <50% found that the former group had a greater percentage of CGR compared to the latter (9.38% vs.

3.57%) as well as an increased median survival (3.45 vs. 2.05 years;  $p < 0.001$ ) [33]. Prior studies have noted superior survival outcomes in high-volume centers [9]. As we demonstrate in this report better outcomes may be attributed to higher CGR rates. Better oncologic outcomes in high-volume centers may also be related to adherence to treatment guidelines, as well as increased ability to salvage patients who experience complications related to cancer treatment [34].

Certain limitations of the present study should be mentioned. Information on individual surgeon's experience (annual volume, number of cases logged, and years of experience) was not available in the National Cancer Database for additional stratification. Similarly, we were unable to identify specific details on the pre-operative tumor burden (size, location, and extent of organ involvement) and details of the exact surgical procedures performed for additional analysis. Moreover, categorization of the surgical procedures to "simple" and "complex" was based on CPT codes that can be associated with coding errors given the subjective nature. Calculation of surgical volume was made by including any patient with stage III-IV who underwent surgery at the reporting facility, thus it may have included a small number of patients with stage IIIA disease who had staging and not cytoreductive surgery. Finally, the grading of CGR and versus macroscopic residual disease has inherent unmeasured bias as this is determined by the operating surgeon.

This is the largest cohort investigating the association between surgical volume and complete gross resection following primary debulking surgery. Results of the present study demonstrate that hospital surgical volume may be associated with the likelihood of achieving complete gross resection following primary debulking surgery supporting the centralization of care in high volume centers. Further research is needed to identify factors associated with superior outcomes in high-volume centers.

#### Author contributions

DN: conception, statistical analysis, critical analysis, drafting/final editing.

RK: critical analysis, drafting/final editing.

ECD: critical analysis, drafting/final editing.

MKF: critical analysis, drafting/final editing.

TAC: critical analysis, drafting/final editing.

SSW: critical analysis, drafting, final editing.

KMH: supervision, critical analysis, drafting, final editing.

#### Declaration of Competing Interest

Nothing to declare.

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