Published in final edited form as:

Int J Gynecol Cancer. 2018 September ; 28(7): 1427–1431. doi:10.1097/IGC.0000000000001315.

Predictors of Unplanned Reoperation for Ovarian Cancer Patients from the National Surgical Quality Improvement Program Database*

Michael D. Toboni, MD, MPH¹, Haller J. Smith, MD², Sejong Bae, PhD³, J. Michael Straughn Jr., MD², and Charles A. Leath III, MD, MSPH²

¹University of Alabama at Birmingham Department of Obstetrics & Gynecology, Birmingham, AL, United States of America

²University of Alabama at Birmingham Division of Gynecologic Oncology, Birmingham, AL, United States of America

³University of Alabama at Birmingham Division of Preventative Medicine, Birmingham, AL, United States of America

Abstract

Objectives—To determine preoperative risk factors associated with unplanned reoperation within 30 days for patients undergoing major surgery for primary ovarian cancer using the National Surgical Quality Improvement Program database (NSQIP) database.

Methods/Materials—We conducted a retrospective cohort study utilizing the NSQIP database to identify patients undergoing primary ovarian cancer surgery from 2012–2014. Patients who had a reoperation within 30 days of their primary surgery were identified. Demographics and clinical covariates were calculated. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated using univariate and multivariate logistic regression approaches to assess the association.

Results—A total of 4,260 patients were identified during the study period. 148 patients (3.5%) underwent a reoperation within 30 days of their primary surgery. In univariate analysis, preoperative creatinine 1.5 mg/dl ($p=0.010$), smoking ($p=0.003$), and both insulin-dependent (IDDM) ($p=0.029$) and non-insulin-dependent diabetes (NIDDM) ($p=0.048$) were predictive of a reoperation. Multivariate analysis noted that smoking OR 1.94 (95% CI 1.26–2.99), IDDM OR 2.18 (95% CI 1.08–4.40), NIDDM OR 1.65 (95% CI 1.01–2.72) and preoperative creatinine OR 2.65 (95% CI 1.26–5.58) were predictive of a reoperation. Age 50 to 60 years was protective against reoperation when compared to age less than 50 OR 0.54 (0.32–0.90).

Conclusions—Efforts to reduce reoperation rates should focus on identifying high-risk patients by utilizing objective preoperative data. Optimizing their medical status prior to surgery may

*Presented in part at the 2017 Society of Gynecologic Oncology Annual Meeting on Women's Cancer, National Harbor, Maryland 2017

Corresponding Author: Michael D. Toboni, MD, MPH University of Alabama at Birmingham, 619 19th Street South, 176F Room 5329, Birmingham AL, 35249, mdtoboni@uabmc.edu Phone: 205-934-7873 Fax: 205-975-6174.

The authors attest that they have no conflicts of interest to disclose.

decrease the reoperation rate in patients with ovarian cancer, thereby improving outcomes and providing a probable cost benefit.

Keywords

NSQIP; Unplanned Reoperation; Ovarian Cancer

Introduction

The need for surgical reoperation in close proximity to an initial operation carries a significant risk of severe morbidity and postoperative mortality. While reoperation rates and resultant morbidity and mortality differ across specialties, patients who undergo the stress of a second operation universally have worse outcomes [1–4]. In a large single center study spanning all surgical specialties, reoperation carried a 21.9% risk of postoperative mortality [1]. Birkmeyer et al. demonstrated an overall reoperation rate of 3.5% in general surgery patients with a disproportionate number of those cases coming from a small number of procedures, including 18.0% from colon resection[3]. In 2013, Clark et al. noted that the reoperation rate for patients with stage II–IV ovarian cancer undergoing a primary cytoreduction via laparotomy was comparable to that seen in the general surgery population at 5.2% [5].

There are substantial risks associated with reoperation across all surgical specialties, and given the significant contribution of reoperation to 30-day readmission rates, it is an important target for quality improvement. Multiple studies have evaluated causes as well as cost attributed to readmissions in gynecology oncology patients. In two single center studies, cost for each readmission ranged from \$8,000 to \$9,300, while the main causes for readmission were infection, wound complications, and small bowel obstructions, all of which could necessitate reoperation[6–8]. In a similar study, diabetes, obesity, smoking, renal co-morbidities, and ASA class over 3 were identified as risk factors for surgical site infections (SSI) in women undergoing hysterectomies, which are risk factors for readmission [9].

Identifying the factors associated with reoperation may allow for improved perioperative management of patients at the highest risk, thereby reducing the rate of reoperation, improving patient outcomes, and providing a cost benefit. The objective of this study was to determine preoperative factors associated with unplanned reoperation within 30 days in patients undergoing major surgery for primary ovarian cancer using the National Surgical Quality Improvement Program database (NSQIP) database.

Materials and Methods

Data Source and Patient Selection

The NSQIP database was used to identify all patients undergoing laparotomy for the primary treatment of ovarian cancer from January 2012 to December 2014. The NSQIP database is a large national database first validated by Khury et al. in 1994 and has been established as the standard for measuring surgical outcomes [10]. Patients were identified using the following

6 common Current Procedural Terminology (CPT) codes for ovarian cancer: 58943 (Oophorectomy, P&P node sampling, peritoneal biopsies/washings +/- salpingectomy +/- omentectomy), 58950 (BSO Omentectomy), 58951 (TAH/BSO, omentectomy, pelvic lymphadenectomy, limited para-aortic lymphadenectomy), 58952 (BSO, omentectomy, debulking (radical dissection)), 58953 (TAH/BSO, omentectomy, debulking (radical dissection)), and 58954 (TAH/BSO, omentectomy, debulking (radical dissection), pelvic lymphadenectomy, limited para-aortic lymphadenectomy). Data is comprised from patients undergoing a primary laparotomy for ovarian cancer.

Variables and Outcomes

Baseline preoperative demographics and clinical characteristics were analyzed. The primary outcome was reoperation within 30 days of primary surgery. The following demographics and clinical covariates were identified as potential risk factors based on clinical experience as well as rationale from the existing literature: age, ASA class 3 or 4, race, tobacco use, preoperative hematocrit <26%, preoperative creatinine >1.5 mg/dl, diabetes (IDDM and NIDDM), and BMI >40 kg/m².

Statistical Analysis

Frequencies and percentages were calculated for categorical variables. In order to assess differences in clinical covariates among patients undergoing reoperation within 30 days of primary operation, we estimated both unadjusted and adjusted odds ratios (OR) and their corresponding 95% confidence intervals (95% CI) using logistic regression analyses in order to prevent bias and potential confounders. Type III analysis of effect P-values were calculated to examine overall categorical differences across covariates in the model. Statistical analyses were performed using SAS v9.4 (SAS Institute, Cary, NC), where statistical significance was considered if p-values were less than 0.05.

Results

4,260 patients underwent a laparotomy for primary treatment of ovarian cancer during the study period. Demographic information is depicted in Table 1. One hundred and forty eight (3.5%) patients required reoperation within 30 days of their primary surgery. Over 55% of the patients were greater than 60 years old with a mean age of 60.4 years. The mean preoperative albumin for all patients, regardless of the need for reoperation, was similar at 3.9 g/dL and thus not selected as a variable.

Both in our univariate and multivariate analysis, three major risk factors were isolated as independent risk factors of reoperation within 30 days: elevated preoperative creatinine (>1.5 mg/dl), smoking (>10 cigarettes/day), and diabetes (both IDDM and NIDDM) (Tables 2, 3). There was no association between reoperation and race, preoperative hematocrit, BMI, or ASA class. Increasing age was not a risk factor for reoperation, in fact, the risk of reoperation for patients age 50–60 was significantly lower than for patients less than age 50 (Table 3).

There were several indications for reoperation, which are detailed in Table 4. There were 189 indications for reoperation in the 148 patients requiring a reoperation as some patients

had multiple indications for a reoperation. Ninety-two percent of the reoperations were at least in part due to bleeding or infection postoperatively. The most common indication for reoperation was bleeding (41.8%) requiring transfusion either intraoperatively or postoperatively. Both preoperative sepsis (4.2%) and postoperative sepsis (12.7%) were significant contributors to reoperation. Infection, which was stratified into superficial (6.3%), deep (7.4%), and organ space infection (19.6%), was also a common reason for reoperation.

Discussion

The overall rate of reoperation after primary surgical treatment of ovarian cancer for patients in the NSQIP database from 2012–2014 was 3.5%, which is consistent with previous estimates in ovarian cancer and general surgery patients [3]. Using the NSQIP database we identified three independent risk factors for unplanned reoperation within 30 days of initial surgery, which include preoperative creatinine above 1.5 mg/dl, smoking more than 10 cigarettes a day, and both non-insulin and insulin-dependent diabetes.

It has been well established that smoking worsens perioperative outcomes. This is in part due to altering migration and destruction of fibroblasts, which are important to healing [11]. In a 2011 study, Alparslan et al. examined postoperative patients and smoking within 30 days of primary surgery and found that smokers had increased deep and superficial infections, organ space infections, bleeding, septic shock, pulmonary embolism, and pneumonia [12]. More specifically, smoking was found to significantly increase anastomotic breakdown in patients healing from esophagogastric cancer [13], which is a concern for gynecologic oncologists who routinely perform bowel surgery.

Similarly to smoking, diabetes has been established as a risk factor for poor healing because of its immunologic and vasculopathic effects [14]. Several factors prevent wound healing in diabetic patients including impaired macrophage function, a variety of growth factors, and decreased angiogenesis. Tissue biopsies have showed increased expression of c-myc and beta-catenin, which inhibited proper wound healing in diabetic foot ulcers by a variety of mechanisms including fibroblast inactivation [15, 16]. Cancienne et al. found that HbA1c values above 7.5% significantly increased infections after lumbar decompression surgery [17]. Although HbA1c would have been an excellent marker for both the presence of and severity of diabetes in our study, NSQIP did not collect this variable during the study time period. Nevertheless, poorly controlled diabetes clearly increases the chances of postoperative complications, including infection and sepsis, which were major causes of reoperation in this population.

The impact of impaired renal function, as evidenced by increased baseline creatinine values has also previously been evaluated. The use of insulin for diabetes and preoperative serum creatinine above 2.0 mg/dL have been independently associated with major cardiac complications during non-cardiac surgery [18]. A subsequent meta-analysis confirmed the observation showing chronic kidney disease is a risk factor for death or cardiac event postoperatively [19]. Similarly, increases in preoperative creatinine were significantly associated with postoperative morbidity and mortality, which included infectious causes and

significant bleeding. These risks were increased in postoperative patients based on creatinine >1.5 mg/dL, and even more so for patients with a creatinine >3.0 mg/dL [20]. Canedo et al. found that patients with chronic kidney disease stage 3 or 4 undergoing colorectal surgery had a higher incidence of SSI [21]. The glomerular filtration rate (GFR) the authors used to characterize these patients corresponds to a creatinine of 1.5, which is also used to predict major adverse cardiac events [22].

Lastly, older age was protective against reoperation in our population. Patients who were 50 to 60 years old were less likely to undergo reoperation when compared to patients under age 50, and while not statistically significant, there was a similar trend in the two older age brackets. Interestingly, a study looking at patients undergoing pancreatic surgery also found younger age to be a risk factor [4]. It is logical to think Surgeons are more likely to be aggressive in younger patients which may lead to greater blood loss, longer surgery times, and more radical surgery to remove tumor. A more aggressive surgical approach may predispose younger patients to reoperation.

Our findings suggest that elevated creatinine, diabetes, and smoking, which are potentially modifiable risk factors, are significantly associated with reoperation in ovarian cancer patients undergoing primary cytoreduction. In this population, BMI, increased ASA class, race, and preoperative hematocrit were not associated with reoperation. There were some limitations to the study. First, we evaluated only patients who had a laparotomy; therefore, the data may not apply to patients undergoing minimally invasive surgery. Similarly, we did not evaluate other gynecologic malignancies besides ovarian, so these preoperative risk factors may not apply to the entire field of gynecologic oncology. Additionally, it is difficult to determine if these patients had received neoadjuvant chemotherapy. Numerous studies have demonstrated a significant increase in postoperative adverse events and mortality in patients undergoing primary surgery compared to neoadjuvant chemotherapy [17, 18], although neoadjuvant chemotherapy is considered to be a negative prognostic factor. Lastly, although we were able to stratify individuals with insulin-dependent and non-insulin-dependent diabetes, we did not have data on Hb1Ac levels.

In summary, efforts to reduce reoperation rates should focus on identifying high-risk patients by utilizing objective preoperative data isolated in this study. Although the presence of risk factors such as these should not be utilized solely to assign a patient to neoadjuvant chemotherapy rather than primary cytoreductive surgery, they warrant further study. Avoiding surgery or optimizing medical comorbidities in these high-risk patients prior to surgery may decrease the reoperation rate, therefore decreasing morbidity and mortality, as well as improving surgical outcomes.

Acknowledgments

Funding: Funding support was provided in part by NIH 3P30CA013148-43S3 and U10CA180855 to CAL.

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Table 1

Study Population (N=4,260)

Reoperation			
	Yes 148 (3.5%)	No 4,112 (96.5%)	% of Total
Age			
<50 years	33 (4.4%)	763 (95.6%)	18.7%
50 to 60 years	28 (2.6%)	1,086 (97.4%)	26.2%
60 to 70 years	40 (3.1%)	1,298 (96.9%)	31.4%
70+ years	47 (3.9%)	965 (95.1%)	23.7%
Race			
White	105 (3.6%)	2,886 (96.4%)	70.2%
Black	9 (3.1%)	292 (96.9%)	7.1%
Asian	8 (3.3%)	246 (96.7%)	5.9%
Hispanic	6 (2.3%)	266 (97.7%)	10.4%
Other	20 (4.7%)	422 (95.3%)	6.4%
BMI (kg/m²)			
>40	16 (4.6%)	347 (95.4%)	8.6%
<40	131 (3.5%)	3,745 (96.5%)	91.4%
Hematocrit			
<26%	6 (7.2%)	83 (92.8%)	2.1%
>26%	141 (3.6%)	3,931 (96.4%)	97.9%
Creatinine (mg/dl)			
<1.5	131 (3.4%)	3,808 (94.6%)	97.8%
>1.5	8 (10.0%)	80 (90.0%)	2.2%
ASA Class			
1&2	60 (3.3%)	1,794 (97.6%)	43.6%
3&4	88 (3.8%)	2,313 (96.2%)	56.4%
Smoker			
No	120 (3.3%)	3,597 (96.7%)	87.3%
Yes	28 (5.4%)	515 (94.6%)	12.7%
Diabetes			
No Diabetes	118 (3.2%)	3,602 (96.8%)	87.3%
IDDM	9 (6.8%)	133 (93.2%)	3.3%
NIDDM	21 (5.6%)	377 (94.4%)	9.4%

IDDM - Insulin dependent diabetes mellitus; NIDDM - Non-insulin dependent diabetes mellitus

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Table 2

Predictors of Reoperation Using a Univariate Logistic Regression

Identified Risk Factors	P-value
Age 50 to 60 years *	0.018
Age 60 to 70 years *	0.071
Age 70 + *	0.913
Creatinine (>1.5 mg/dl vs. <1.5 mg/dl)	0.010
Hematocrit (>26% vs. <=26%)	0.094
IDDM **	0.029
NIDDM **	0.048
BMI (<40 kg/m ² vs. >=40 kg/m ²)	0.486
ASA Class (1&2 vs. 3&4)	0.801
Smoking	0.003
Asian	0.922
Hispanic	0.344
Non-Hispanic Black	0.599
Other	0.197

IDDM – Insulin-dependent diabetes mellitus; NIDDM - Non-insulin-dependent diabetes mellitus

Bolded rows indicate statistical significance

* Compared to age <50 years

** Compared to patients without diabetes

Table 3

Predictors of Reoperation Using a Multivariate Logistic Regression

Identified Risk Factors	OR	95% Confidence Intervals	
Age 50 to 60 years *	0.535	0.318	0.899
Age 60 to 70 years *	0.640	0.395	1.040
Age 70 + *	0.973	0.594	1.595
Creatinine (>1.5 mg/dl vs. <1.5 mg/dl)	2.651	1.259	5.582
Hematocrit (>26% vs. ≤26%)	0.493	0.216	1.129
IDDM **	2.182	1.082	4.400
NIDDM **	1.652	1.004	2.719
BMI (<40 kg/m ² vs. ≥40 kg/m ²)	0.819	0.466	1.438
ASA Class (1&2 vs. 3&4)	1.048	0.728	1.508
Smoking	1.942	1.260	2.992
Asian	0.962	0.448	2.069
Hispanic	0.678	0.303	1.517
Non-Hispanic Black	0.833	0.422	1.644
Other	1.387	0.844	2.279

IDDM – Insulin-dependent diabetes mellitus; NIDDM - Non-insulin-dependent diabetes mellitus

Bolded rows indicate statistical significance

* Compared to age <50 years

** Compared to patients without diabetes

Table 4

Indications for Reoperation (N=189)

Cited Indication for Reoperation	Number	% of total
Bleeding	79	(41.8%)
Organ Space Infection	37	(19.6%)
Postoperative Sepsis	24	(12.7%)
Deep Incisional Infection	14	(7.4%)
Superficial Incisional Infection	12	(6.3%)
Preoperative Sepsis	8	(4.2%)
Renal Insufficiency	8	(4.2%)
Other	7	(3.8%)

*
 Requiring a transfusion intraoperatively or postoperatively