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# Risk Stratification and Outcomes of Women Undergoing Surgery for Ovarian Cancer

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## Abstract

**Objective—**Cytoreduction for ovarian cancer is associated with substantial morbidity. We examined the outcome of patients undergoing surgery for ovarian cancer to determine if there are sub-groups of patients who may benefit from alternative treatments.

**Methods—**The National Surgical Quality Improvement Program database was used to identify women who underwent surgery for ovarian cancer from 2005–2012. Multivariable logistic regression models were used to examine the effect of age, race, functional status, ASA class, preoperative albumin and performance of extended cytoreductive procedures on morbidity, mortality and resource utilization.

**Results—**A total of 2870 women were identified. The perioperative complication rate increased from 9.5% in women <50 years, to 13.4% in those age 60–69 years, and 14.6% in women ≥70 years (P<0.0001). Similarly, complications rose from 7.3% in those who did not require any extended procedures to 12.9% after 1 procedure, 28.4% for those who had 2, and 30.0% in women who underwent ≥3 extended procedures (P<0.0001). In a series of multivariable models, the number of extended cytoreductive procedures performed and preoperative albumin were the



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**Conflict of Interest**

The authors have no conflicts of interest.

factors most consistently associated with morbidity. Using a series of model fit statistics, compared to chance alone, the ability to predict any complication increased by 27.4% when procedure score was analyzed, 22.0% with preoperative albumin, 11% with age, and 4% with functional status.

**Conclusions—**While preoperative clinical and demographic factors may help predict the risk of adverse outcomes for women undergoing surgery for ovarian cancer, performance of extended cytoreductive procedures is the strongest risk factor for complications.

## Introduction

Primary cytoreduction followed by platinum-based combination chemotherapy is the standard of care for the treatment of advanced stage, epithelial ovarian cancer.[1] Surgical cytoreduction entails salpingo-oophorectomy, typically with hysterectomy, omentectomy and resection of gross tumor within the abdominal cavity. Resection of tumor may require small or lrge bowel resection as well as removal of other solid organs, including the liver and spleen.[2–4] Multiple studies have demonstrated that the amount of residual tumor after completion of the surgery is associated with long-term prognosis.[4–7] Patients who are suboptimally cytoreduced prior to chemotherapy have decreased survival.[2,8,9]

Although cytoreductive surgery has numerous benefits, the operation is associated with significant morbidity.[10–13] A number of prior studies have attempted to define factors that are associated with excessive morbidity in women undergoing cytoreduction.[12] Several reports have noted that advanced age is associated with adverse outcomes.[11,12,14] However, some studies have suggested that chronologic age alone should not be a contraindication to cytoreduction and that measures of performance status and functional reserve are of greater importance.[15,16]

In addition to age, the extent of cytoreductive surgery appears to influence outcomes. Prior work has shown that complications increase with the number of radical procedures performed.[12] Given the increased morbidity associated with factors such as the requirement for more extensive cytoreductive surgery and advance age, some reports have suggested that patients with these factors may benefit from alternative treatment strategies such as neoadjuvant chemotherapy.

The objective of our study was to examine the influence of age, functional status, and extent of cytoreduction on perioperative morbidity in women with ovarian cancer. Specifically, we utilized a large, population-based database that prospectively collects detailed clinical characteristics and outcomes for patients from throughout the United States.

## Materials and Methods

### Data source and patient selection

We examined the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) database.[17,18] The NSQIP database is a risk-adjusted, nationally validated and prospectively maintained surgical outcomes registry. It contains more than 240 clinical variables, including preoperative patient characteristics, intraoperative variables and 30-day postoperative outcomes. All data is abstracted from medical records by trained registrars using a highly structured sampling schema. The Columbia University Institutional Review Board deemed the study exempt.

Women ≥18 years of age with ovarian cancer (ICD-9 183.x) recorded from 2005–2012 were included. The study cohort was limited to only those patients who underwent an ovarian cancer directed surgery defined hysterectomy, oophorectomy, cystectomy or tumor cytoreduction (Supplemental Table 1).

The type and number of additional extended procedures each patient underwent were recorded. The procedures of interest included lymphadenectomy, small bowel resection, colectomy, rectosigmoid resection, hepatic resection, bladder resection, diaphragm resection and cytoreduction. In addition to individual procedures, a composite score based on the number of the above extended procedures each patient underwent was calculated. The procedure score was categorized as: 0 procedures, 1 procedure, 2 procedures, and ≥3 procedures.[12]

## Clinical and demographic characteristics

Patients were classified based on age at surgery into the following groups: <50 years of age, 50–59 years, 60–69 years and ≥70 years. Race was categorized as white, black, other or unknown. Body mass index was calculated as the weight (kg) divided by height ($m^2$) and recorded as: normal (<25 kg/$m^2$), overweight (25–29.9 kg/$m^2$), obese (≥30 kg/$m^2$), and unknown.

Covariates potentially associated with performance status including American Society of Anesthesiology (ASA) classification score (1, 2, 3, 4, 5, or unknown), preoperative functional status (independent, partially dependent, totally dependent, and unknown) and preoperative albumin (<3.5 g/dL, 3.5–4 g/dL, and >4 g/dL), were recorded for each patient.[17] The presence of a number of preoperative medical comorbidities including diabetes mellitus (insulin dependent or non-insulin dependent), tobacco use, chronic obstructive pulmonary disease, congestive heart failure, hypertension, corticosteroid use, and the presence of ascites were noted for each patient.[19]

## Outcome variables

The primary outcomes of the study were perioperative morbidity and mortality. Any complication was defined as a composite measure if the patient was noted to have any of the following postoperative complications: pneumonia, acute renal failure, urinary tract infection, cerebrovascular accident, coma, sepsis, shock, cardiac arrest, myocardial infarction, pulmonary embolism, deep venous thrombosis, prolonged mechanical ventilation, unplanned re-intubation, or progressive renal insufficiency.[19] Severe complications were analyzed based on Clavian class IV complications and included shock, cardiac arrest, myocardial infarction, pulmonary embolism, prolonged intubation or unplanned re-intubation.[20–22] Wound complications included superficial or deep surgical site infections or an organ space surgical site infection.[19]

Prolonged length of stay was defined as hospitalization after surgery of >8 days while non-routine discharge was defined as discharge to a rehabilitation or skilled nursing facility. Intraoperative or postoperative transfusion of blood products and readmission within 30-days of the intervention were noted for each patient. Return to the operating room after the primary procedure was defined as reoperation. Perioperative mortality was defined as death within 30-days of the index surgical procedure.[19]

### Statistical analysis

Frequency distributions between categorical variables were compared using $\chi^2$ tests. Clinical and demographic data are reported descriptively stratified by age while outcomes are reported stratified by age and procedure score. Multivariable logistic regression models were developed to examine the association between the clinical and demographic characteristics and the number of extended procedures performed and outcomes. Results are reported with risk ratios and 95% confidence intervals.

A number of model fit statistics were estimated to examine the strength of the model to predict the outcome based on clinical characteristics (age, functional status, preoperative albumin, and procedure score) and outcomes. The area under the receiver operating characteristics (ROC) curve of a plot of the true positive rate (sensitivity) versus the false positive rate was estimated with the c-statistic. The c-statistic represents the ability of a model to accurately predict the outcome. Values for the c-statistic range from 0.5 (model no better than chance in discriminating outcome) to 1 (perfect prediction of the outcome).

The pseudo-$R^2$ is an indicator of the variability in outcome that is explained by the model and is analogous to $R^2$ derived from least squares linear regression. Likelihood ratio tests (LRT) compare the fit of a model with the covariates of interest to a null model (no covariates included). A higher LRT suggests a greater importance of the variable or variables. The Akaike information criterion (AIC) measures the goodness of fit of a model in the context of the overall complexity of the model. A lower AIC suggests greater importance for a variable.

We estimated the ability of a given covariate or set of covariates to distinguish the outcomes of interest. We first assumed that the c-statistic of a null model was 0.5 and the calculated the predictive ability of covariates as: (c-statistic of model with one or more variables)/(c-statistic of null model).[23] Data analysis was performed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina). All statistical tests were two-sided. A P-value of <0.05 was considered to be statistically significant

## Results

A total of 2870 women with ovarian cancer were identified. The cohort included 547 (19.1 %) women < 50 years of age, 784 (27.3 %) women age 50–59, 838 (29.2 %) women age 60–69, and 701 (24.4 %) women ≥70 years of age (Table 1). Compared to their younger counterparts, the older women were more often white, had normal BMIs, had higher ASA class, had lower preoperative albumin and were more likely to be partially dependent. Furthermore, older women were more likely to have preoperative medical comorbidities, such as non-insulin dependent diabetes mellitus, COPD and hypertension (P < 0.05 for all). Women 60–69 and ≥70 were more likely to undergo cytoreduction, small bowel resection and colectomy but less likely to undergo lymphadenectomy (P value < 0.05 for all).

The rate of any perioperative complications increased from 9.5% in women <50 to 9.7% in those 50–59, 13.4% in those aged 60–69, and 14.6% in women ≥70 years of age (P<0.0001). Compared to women <50 years of age, patients ≥70 were at increased risk for prolonged hospitalization (16.5 % vs. 32.5%; P<0.0001), non-routine discharge (2.2 % vs. 16.8 %; P<0.0001), transfusion (26.1% vs. 39.2%; P<0.0001), and death (0.9 % vs. 2.7 %; P<0.001) (Table 2).

When stratified by the number of radical procedures performed during the surgery (0 vs. 1 vs. 2 vs. ≥3), the overall complication rate rose from 7.3% in those who did not require any extended procedures to 12.9% for those who underwent 1 procedure, 28.4% for those who had 2, and 30.0% in women who underwent ≥3 extended procedures (P < 0.0001) (Table 3). Perioperative mortality increased from 0.7% to 2.0% in subjects who underwent 3 or more radical procedures. Prolonged hospitalization, non-routine discharge, transfusion, readmission and reoperation all increased with the number of radical procedures performed (P < 0.05 for all).

In a series of multivariable models corrected for clinical and demographic characteristics, the number of extended cytoreductive procedures performed and preoperative albumin were the factors most consistently associated with perioperative morbidity (Table 4). While advanced age alone was not associated with perioperative complications, women ≥70 years of age and those with higher ASA scores were more likely to require prolonged hospitalization and non-routine discharge (P<0.05), while functional status was associated with prolonged hospitalization, non-routine discharge, and complications. Performance of ≥3 cytoreductive procedures was associated with any complication (RR=4.06; 95% CI, 2.34–7.03), severe complications (RR = 5.07; 95% CI, 2.47–10.41), wound complications (RR=3.80; 95% CI, 1.88–7.69), prolonged hospitalization (RR=4.68; 95% CI, 3.22–6.80), non-routine discharge (RR=2.82; 95% CI, 1.11–7.19) and transfusion (RR=3.15; 95% CI, 2.14–4.63). Similarly, preoperative albumin levels were associated with any complication, severe complications, prolonged hospitalization, nonroutine discharge, transfusion and reoperation (P<0.05 for all). Similarly, preoperative albumin levels were associated with any complication, severe complications, prolonged hospitalization, non-routine discharge, transfusion and reoperation (P<0.05 for all).

We then estimated a number of model fit statistics to determine the importance of each factor in predicting outcomes (Table 5). Compared to chance alone, the ability to predict any complication was increased by 27.4% when procedure score was analyzed, 22.0% with preoperative albumin, 11.0% with age, and 4.0% with functional status. Combining these four measures increased predictive ability to 37.6%, while the full model with all the clinical and demographic characteristics enhanced the predictive ability to 40.4%. The procedure score and preoperative albumin were the most important individual predictors of severe complications, wound complications, readmission, and reoperation, while age was the most important factor in distinguishing readmission.

## Discussion

These findings suggest that the perioperative complication rate for surgery for ovarian cancer is substantial. While age and functional status are associated with outcomes, among patient factors, preoperative albumin level is the strongest predictor of perioperative morbidity. However, the number of extended procedures performed is the most important factor associated with adverse outcomes.

The importance of perioperative surgical complications is now well recognized.[24–26] In a study of over 100,000 patients who underwent major surgery, the occurrence of a complication in the 30-day postoperative period was more important in determining survival than preoperative patient and intraoperative factors.[24] For cancer patients, perioperative complications can lead to delay in the initiation of chemotherapy and increase the risk of omission of chemotherapy that may ultimately impact survival from cancer. In a population-based analysis of women with ovarian cancer, women who experienced a perioperative complication were over 60% more likely to not initiate chemotherapy within 6 weeks of surgery.[26]

Somewhat surprisingly, neither age nor functional status was independently associated with morbidity or mortality. In contrast, preoperative albumin levels, a marker of functional reserve, were highly associated with perioperarive outcomes. Other reports have noted similar findings. Langstratt and colleagues found that an albumin level ≤3 was an important predictor of poor perioperative outcomes in women ≥65 undergoing primary debulking surgery for ovarian cancer.[27] Similarly, a second report noted that serum albumin levels ≤3.5g/dL adversely affected survival by a statistically significant level across all stages of ovarian cancer, independent of stage at diagnosis, serum cancer antigen-125 and previous treatment history.[28]

The number of extended cytoreductive proceudres performed was the factor most predictive of perioperative morbidity. Prior work has demonstrated similar findings. In an analysis of over 28,000 women with ovarian cancer the complication rate increased from 20% in patients who underwent no extended procedures to 34% in patients who required one additional procedure and 44% in those requiring 2 or more extended procedures.[12] We noted similar trends for the overall rate of complications, wound complications, severe complications, prolonged hospitalization, transfusion and non-routine discharge.

Given that those women who require multiple extended procedures are at highest risk, these data suggest that alternative treatment strategies should be considered in women who may require extended cytoreductive surgery. However, identification of women who may require extended cytoreduction has often proven difficult. Reports examining the ability of various imaging modalities to predict resectable have reported mixed results.[29–31] More recently, there has been greater interest in laparoscopic assessment of intraabdominal disease prior to laparotomy.[32]

Given the substantial morbidity associated with cytoreductive surgery for ovarian cancer, there has been great interest in strategies to reduce perioperative complications. A number of studies of neoadjuvant chemotherapy have suggested that preoperative chemotherapy reduces the extent of surgery required for women with ovarian cancer as well as complications.[10,33–36] In an institutional series of 172 patients with advanced stage ovarian cancer, radical organ resections were required in 25% of women who underwent primary cytoreduction compared to only 6% of those who received neoadjuvant chemotherapy.[33] In a prospective trial comparing neoadjuvant chemotherapy and primary cytoreduction, the rate of hemorrhagic (4% vs. 7%) and infectious (8% vs. 2%) complications were lower in women in women who received neoadjuvant chemotherapy.[10] Perhaps most importantly, the perioperative mortality rate was nearly four times higher among women who underwent primary cytoreduction.[10]

While neoadjuvant chemotherapy is associated with decreased perioperative morbidity, whether this strategy is associated with reduced long-term survival remains an area of active debate.[10,11,37–39] A randomized phase III trial of neoadjuvant chemotherapy compared to cytoreductive surgery noted equivalent survival for the two strategies. The amount of residual tumor after surgery, but not the timing of surgery, was predictive of survival.[10] This trial has been criticized in that survival was lower than in many contemporaneous groups of patients treated in the U.S. and the overall rate of optimal cytoreduction was low. Given the substantial risk of morbidity for patients who require multiple organ resections at the time of cytoreduction, these women may derive particular benefit for neoadjuvant chemotherapy.[38]

We recognize a number of important limitations. First, we lack data on tumor characteristics, prior surgical history, and extent of disease. Tumor stage as well as the volume and distribution of tumor implants within the abdomen likely impact not only extent of surgery, but also perioperative outcomes. Second, we are only able to capture 30-day perioperative outcomes. While data on long-term outcomes would be of interest, a priori the goal of our analysis was to examine how clinical and demographic factors influenced near term outcomes. As described, prior work has shown the association with perioperative complications and receipt of chemotherapy and survival.[24–26] Third, we cannot exclude the possibility that some complications were not captured. However, a strength of the NSQIP dataset is the thorough capture of perioperative events. As such, the dataset is well suited to the current study. Although a variable for preoperative chemotherapy exists within the dataset, this variable was missing for a large number (46.0%) of the patients in our cohort. We therefore cannot accurately distinguish primary from interval cytoreduction. Lastly, as with any study of administrative data, we were unable to capture data on individual patient and physician preferences that undoubtedly influenced surgical planning and outcomes.

In sum, these findings suggest that the number of extended surgical procedures and preoperative albumin are the strongest predictors of adverse perioperative outcomes in women with ovarian cancer. As such, those women who may require extended cytoreduction, particularly those with poor performance status and low albumin levels, may benefit from alternative treatment strategies such as neoadjuvant chemotherapy.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Research Highlights**

- Surgery for ovarian cancer is associated with substantial morbidity.
- While preoperative clinical and demographic factors may help predict the risk of adverse outcomes for women undergoing surgery for ovarian cancer,
- performance of extended cytoreductive procedures is the strongest risk factor for complications.
- Alternative treatment strategies may be considered in women with ovarian cancer at high risk for complications.

**Table 1**

Clinical and demographic characteristics of the cohort stratified by age at surgery.

| | <50 years | | 50–59 years | | 60–69 years | | ≥70 years | | *P-value* |
|---|---|---|---|---|---|---|---|---|---|
| | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | |
| | 547 | (19.1) | 784 | (27.3) | 838 | (29.2) | 701 | (24.4) | |
| *Year of procedure* | | | | | | | | | 0.08 |
| 2005–2006 | 5 | (0.9) | 7 | (0.9) | 5 | (0.6) | 10 | (1.4) | |
| 2007 | 8 | (1.5) | 23 | (2.9) | 22 | (2.6) | 25 | (3.6) | |
| 2008 | 33 | (6.0) | 49 | (6.3) | 41 | (4.9) | 46 | (6.6) | |
| 2009 | 68 | (12.4) | 70 | (8.9) | 88 | (10.5) | 51 | (7.3) | |
| 2010 | 74 | (13.5) | 98 | (12.5) | 107 | (12.8) | 81 | (11.6) | |
| 2011 | 166 | (30.4) | 241 | (30.7) | 251 | (30.0) | 221 | (31.5) | |
| 2012 | 193 | (35.3) | 296 | (37.8) | 324 | (38.7) | 267 | (38.1) | |
| *Race* | | | | | | | | | 0.0003 |
| White | 388 | (70.9) | 575 | (73.3) | 661 | (78.9) | 540 | (77.0) | |
| Black | 52 | (9.5) | 56 | (7.1) | 37 | (4.4) | 45 | (6.4) | |
| Other | 27 | (4.9) | 30 | (3.8) | 19 | (2.3) | 15 | (2.1) | |
| Unknown | 80 | (14.6) | 123 | (15.7) | 121 | (14.4) | 101 | (14.4) | |
| *BMI* | | | | | | | | | <0.0001 |
| Normal | 202 | (36.9) | 275 | (35.1) | 275 | (32.8) | 276 | (39.4) | |
| Overweight | 136 | (24.9) | 195 | (24.9) | 258 | (30.8) | 238 | (34.0) | |
| Obese | 197 | (36.0) | 302 | (38.5) | 300 | (35.8) | 185 | (26.4) | |
| Unknown | 12 | (2.2) | 12 | (1.5) | 5 | (0.6) | 2 | (0.3) | |
| *ASA Class* | | | | | | | | | <0.0001 |
| 1 | 43 | (7.9) | 33 | (4.2) | 15 | (1.8) | 3 | (0.4) | |
| 2 | 287 | (52.5) | 399 | (50.9) | 347 | (41.4) | 228 | (32.5) | |
| 3 | 204 | (37.3) | 330 | (42.1) | 440 | (52.5) | 433 | (61.8) | |
| ≥4 | 12 | (2.2) | 21 | (2.7) | 36 | (4.3) | 37 | (5.3) | |
| Unknown | 1 | (0.2) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | |
| *Functional status* | | | | | | | | | 0.02 |
| Independent | 531 | (97.1) | 770 | (98.2) | 824 | (98.3) | 668 | (95.3) | |

| | <50 years | | 50–59 years | | 60–69 years | | ≥70 years | | *P-value* |
|---|---|---|---|---|---|---|---|---|---|
| | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | |
| Partially dependent | 11 | (2.0) | 11 | (1.4) | 13 | (1.6) | 29 | (4.1) | |
| Totally dependent | 4 | (0.7) | 3 | (0.4) | 1 | (0.1) | 4 | (0.6) | |
| Unknown | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | |
| *Modified frailty index* | | | | | | | | | |
| Median (IQR) | 0 (0-0) | | 0 (0–0.09) | | 0.09 (0–0.2) | | 0.09 (0–0.2) | | |
| *Preoperative albumin* | | | | | | | | | <0.0001 |
| <3.5 | 82 | (15.0) | 117 | (14.9) | 144 | (17.2) | 153 | (21.8) | |
| 3.5–4 | 120 | (21.9) | 179 | (22.8) | 220 | (26.3) | 207 | (29.5) | |
| >4 | 164 | (30.0) | 237 | (30.2) | 216 | (25.8) | 158 | (22.5) | |
| Unknown | 181 | (33.1) | 251 | (32.0) | 258 | (30.8) | 183 | (26.1) | |
| *Preoperative conditions* | | | | | | | | | |
| Insulin dependent diabetes mellitus | 18 | (3.3) | 23 | (2.9) | 21 | (2.5) | 18 | (2.6) | <0.0001 |
| Non-insulin dependent diabetes mellitus | 18 | (3.3) | 43 | (5.5) | 82 | (9.8) | 86 | (12.3) | <0.0001 |
| Tobacco use | 116 | (21.2) | 131 | (16.7) | 103 | (12.3) | 48 | (6.9) | <0.0001 |
| COPD | 3 | (0.6) | 11 | (1.4) | 27 | (3.2) | 35 | (5.0) | <0.0001 |
| Ascites | 104 | (19.0) | 151 | (19.3) | 213 | (25.4) | 154 | (22.0) | 0.03 |
| CHF | 0 | (0.0) | 4 | (0.5) | 2 | (0.2) | 6 | (0.9) | 0.06 |
| Hypertension | 84 | (15.4) | 242 | (30.9) | 405 | (48.3) | 457 | (65.2) | <0.0001 |
| Steroid use | 11 | (2.0) | 19 | (2.4) | 30 | (3.6) | 28 | (4.0) | 0.02 |
| *Concurrent procedures* | | | | | | | | | |
| Lymphadenectomy | 248 | (45.3) | 359 | (45.8) | 320 | (38.2) | 215 | (30.7) | <0.0001 |
| Cytoreduction | 224 | (41.0) | 371 | (47.3) | 458 | (54.7) | 351 | (50.1) | 0.0001 |
| Small bowel resection | 10 | (1.8) | 24 | (3.1) | 25 | (3.0) | 32 | (4.6) | 0.01 |
| Colectomy | 11 | (2.0) | 17 | (2.2) | 37 | (4.4) | 41 | (5.9) | <0.0001 |
| Rectosigmoid resection | 15 | (2.7) | 47 | (6.0) | 55 | (6.6) | 37 | (5.3) | 0.07 |
| Hepatic resection | 8 | (1.5) | 12 | (1.5) | 14 | (1.7) | 10 | (1.4) | 0.99 |
| Bladder resection | 1 | (0.2) | 1 | (0.1) | 2 | (0.2) | 0 | (0.0) | 0.52 |
| Diaphragm resection | 10 | (1.8) | 11 | (1.4) | 20 | (2.4) | 11 | (1.6) | 0.86 |
| *Extended procedure score* | | | | | | | | | <0.0001 |
| 0 | 309 | (56.5) | 396 | (50.5) | 342 | (40.8) | 305 | (43.5) | |

| | <50 years | | 50–59 years | | 60–69 years | | ≥70 years | | *P-value* |
|---|---|---|---|---|---|---|---|---|---|
| | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | **N** | **(%)** | |
| 1 | 201 | (36.8) | 300 | (38.3) | 394 | (47.0) | 319 | (45.5) | |
| 2 | 30 | (5.5) | 75 | (9.6) | 84 | (10.0) | 65 | (9.3) | |
| >3 | 7 | (1.3) | 13 | (1.7) | 18 | (2.2) | 12 | (1.7) | |

## Table 2

Perioperative outcomes stratified by age at surgery.

| | <50 years | | 50–59 years | | 60–69 years | | ≥70 years | | *P-value* |
|---|---|---|---|---|---|---|---|---|---|
| | N | (%) | N | (%) | N | (%) | N | (%) | |
| *Complications* | | | | | | | | | |
| Any complication | 52 | (9.5) | 76 | (9.7) | 112 | (13.4) | 102 | (14.6) | 0.0007 |
| Wound complication | 36 | (6.6) | 45 | (5.7) | 67 | (8.0) | 45 | (6.4) | 0.61 |
| Severe complication | 30 | (5.5) | 40 | (5.1) | 63 | (7.5) | 63 | (9.0) | 0.0023 |
| *Resource utilization* | | | | | | | | | |
| Prolonged hospitalization[1] | 90 | (16.5) | 171 | (21.8) | 214 | (25.5) | 228 | (32.5) | <0.0001 |
| Non-routine discharge[2] | 8 | (2.2) | 17 | (3.2) | 37 | (6.4) | 82 | (16.8) | <0.0001 |
| Transfusion[3] | 113 | (26.1) | 199 | (31.3) | 242 | (35.5) | 223 | (39.2) | <0.0001 |
| Readmission[2] | 35 | (9.8) | 55 | (10.2) | 56 | (9.7) | 56 | (11.5) | 0.48 |
| Reoperation | 24 | (4.4) | 30 | (3.8) | 25 | (3.0) | 26 | (3.7) | 0.57 |
| *Death* | 5 | (0.9) | 3 | (0.4) | 10 | (1.2) | 19 | (2.7) | 0.0009 |

[1] Hospitalization ≥8 days

[2] Data only available from 2011–2012

[3] Data only available from 2010–2012

## Table 3

Perioperative outcomes stratified by number of extended procedures performed.

| | 0 procedures | | 1 procedure | | 2 procedures | | ≥3 procedures | | *P-value* |
|---|---|---|---|---|---|---|---|---|---|
| | N | (%) | N | (%) | N | (%) | N | (%) | |
| *Complications* | | | | | | | | | |
| Any complication | 99 | (7.3) | 156 | (12.9) | 72 | (28.4) | 15 | (30.0) | <0.0001 |
| Wound complication | 68 | (5.0) | 80 | (6.6) | 36 | (14.2) | 9 | (18.0) | <0.0001 |
| Severe complication | 51 | (3.8) | 92 | (7.6) | 44 | (17.3) | 9 | (18.0) | <0.0001 |
| *Resource utilization* | | | | | | | | | |
| Prolonged hospitalization[1] | 201 | (14.9) | 323 | (26.6) | 146 | (57.5) | 33 | (66.0) | <0.0001 |
| Non-routine discharge[2] | 46 | (5.3) | 72 | (8.5) | 21 | (10.6) | 5 | (13.2) | 0.0006 |
| Transfusion[3] | 224 | (21.3) | 368 | (37.3) | 155 | (65.1) | 30 | (68.2) | <0.0001 |
| Readmission[2] | 75 | (8.6) | 94 | (11.1) | 28 | (14.1) | 5 | (13.2) | 0.01 |
| Reoperation | 41 | (3.0) | 39 | (3.2) | 22 | (8.7) | 3 | (6.0) | 0.001 |
| *Death (global death)* | 9 | (0.7) | 17 | (1.4) | 10 | (3.9) | 1 | (2.0) | 0.0002 |

[1] Hospitalization ≥8 days

[2] Data only available from 2011–2012

[3] Data only available from 2010–2012

**Table 4**

Multivariable models of perioperative morbidity and resource utilization.

| | Wound complication | Severe complication | Any complication | Prolonged hospitalization | Non-routine discharge[1] | Transfusion[2] | Readmission[1] | Reoperation |
|---|---|---|---|---|---|---|---|---|
| *Age* | | | | | | | | |
| <50 | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| 50–59 | 0.77 (0.49, 1.19) | 0.84 (0.52, 1.35) | 0.93 (0.65, 1.33) | 1.24 (0.96, 1.60) | 1.39 (0.60, 3.22) | 1.10 (0.88, 1.39) | 0.99 (0.65, 1.52) | 0.80 (0.46, 1.38) |
| 60–69 | 1.00 (0.66, 1.51) | 1.09 (0.70, 1.71) | 1.15 (0.82, 1.61) | 1.27 (0.99, 1.63) | 2.42 (1.12, 5.24)* | 1.15 (0.92, 1.44) | 0.92 (0.60, 1.42) | 0.59 (0.33, 1.04) |
| ≥70 | 0.83 (0.53, 1.31) | 1.14 (0.73, 1.79) | 1.16 (0.82, 1.63) | 1.46 (1.14, 1.88)* | 5.47 (2.62, 11.42)** | 1.20 (0.95, 1.52) | 1.08 (0.70, 1.67) | 0.67 (0.37, 1.19) |
| *Year of procedure* | | | | | | | | |
| 2005–06 | Referent | Referent | Referent | Referent | NA | NA | NA | Referent |
| 2007 | 0.63 (0.15, 2.55) | 3.97 (0.51, 31.07) | 1.95 (0.43, 8.88) | 1.30 (0.64, 2.67) | NA | NA | NA | 1.95 (0.40, 9.47) |
| 2008 | 0.43 (0.11, 1.73) | 1.09 (0.13, 9.18) | 0.80 (0.17, 3.73) | 0.57 (0.27, 1.20) | NA | NA | NA | 0.43 (0.07, 2.49) |
| 2009 | 0.37 (0.10, 1.43) | 0.82 (0.10, 6.82) | 0.88 (0.20, 3.94) | 0.57 (0.28, 1.18) | NA | NA | NA | 0.45 (0.08, 2.46) |
| 2010 | 0.42 (0.12, 1.52) | 0.91 (0.11, 7.37) | 0.99 (0.23, 4.32) | 0.54 (0.27, 1.10) | NA | Referent | NA | 0.31 (0.06, 1.63) |
| 2011 | 0.47 (0.14, 1.64) | 0.97 (0.12, 7.67) | 0.98 (0.23, 4.20) | 0.44 (0.22, 0.88)* | Referent | 1.10 (0.88, 1.37) | Referent | 0.32 (0.06, 1.63) |
| 2012 | 0.52 (0.15, 1.79) | 0.77 (0.10, 6.07) | 0.92 (0.21, 3.96) | 0.48 (0.24, 0.97)* | 0.86 (0.62, 1.20) | 1.10 (0.89, 1.36) | 0.86 (0.65, 1.13) | 0.28 (0.05, 1.40) |
| *Race* | | | | | | | | |
| White | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| Black | 1.04 (0.61, 1.79) | 1.23 (0.74, 2.02) | 1.15 (0.77, 1.70) | 1.14 (0.87, 1.50) | 1.08 (0.60, 1.96) | 1.19 (0.91, 1.55) | 0.99 (0.56, 1.77) | 0.66 (0.26, 1.64) |
| Other | 1.32 (0.58, 3.03) | 1.74 (0.88, 3.46) | 1.35 (0.77, 2.38) | 1.05 (0.67, 1.63) | 0.46 (0.11, 1.92) | 1.41 (0.99, 2.02) | 1.75 (0.91, 3.38) | 1.80 (0.77, 4.20) |
| Unknown | 0.97 (0.61, 1.55) | 0.53 (0.28, 0.98)* | 0.62 (0.40, 0.95)* | 0.72 (0.53, 0.96)* | 0.62 (0.32, 1.21) | 1.16 (0.93, 1.44) | 1.11 (0.72, 1.72) | 0.61 (0.28, 1.34) |
| *BMI* | | | | | | | | |
| Normal | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| Overweight | 0.98 (0.66, 1.45) | 1.06 (0.75, 1.51) | 1.08 (0.83, 1.40) | 0.98 (0.82, 1.18) | 1.47 (0.96, 2.25) | 0.88 (0.74, 1.05) | 0.95 (0.66, 1.35) | 0.73 (0.46, 1.18) |
| Obese | 1.57 (1.12, 2.22) | 1.00 (0.70, 1.42) | 1.02 (0.78, 1.33) | 0.92 (0.76, 1.10) | 1.56 (1.02, 2.40)* | 0.80 (0.68, 0.96) | 1.14 (0.81, 1.59) | 0.59 (0.36, 0.96)* |
| Unknown | 1.05 (0.25, 4.40) | 0.64 (0.09, 4.66) | 0.67 (0.16, 2.74) | 1.47 (0.77, 2.80) | 1.58 (0.21, 11.60) | 0.77 (0.34, 1.73) | 1.10 (0.27, 4.51) | 1.30 (0.31, 5.49) |
| *ASA Class* | | | | | | | | |
| 1 | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| 2 | 1.45 (0.45, 4.65) | 1.73 (0.42, 7.13) | 1.75 (0.64, 4.76) | 1.38 (0.70, 2.70) | - | 1.51 (0.87, 2.65) | 2.04 (0.64, 6.49) | 1.82 (0.44, 7.59) |
| 3 | 2.06 (0.64, 6.60) | 2.51 (0.61, 10.30) | 2.39 (0.88, 6.49) | 2.06 (1.06, 4.03)* | 1.79 (1.18, 2.71)* | 1.84 (1.05, 3.22) | 2.21 (0.69, 7.08) | 1.89 (0.45, 7.96) |

| | Wound complication | Severe complication | Any complication | Prolonged hospitalization | Non-routine discharge[1] | Transfusion[2] | Readmission[1] | Reoperation |
|---|---|---|---|---|---|---|---|---|
| ≥4 | 2.40 (0.64, 8.91) | 2.58 (0.56, 11.79) | 2.27 (0.75, 6.85) | 3.04 (1.49, 6.24)* | 2.30 (1.13, 4.67)* | 1.95 (1.02, 3.72) | 1.42 (0.33, 6.05) | 2.31 (0.43, 12.33) |
| *Functional status* | | | | | | | | |
| Independent | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| Partially dependent | - | 1.93 (1.06, 3.51)* | 1.52 (0.90, 2.56) | 1.43 (1.02, 2.02) | 3.17 (1.75, 5.74)* | 0.89 (0.55, 1.44) | - | 0.86 (0.26, 2.82) |
| Totally dependent | - | 5.36 (1.91, 15.00)** | 4.01 (1.62, 9.96)* | 2.51 (1.23, 5.12)* | 3.65 (0.86, 15.40) | 2.19 (0.70, 6.88) | - | 2.14 (0.29, 15.88) |
| *Preoperative albumin* | | | | | | | | |
| <3.5 | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| 3.5–4 | 0.85 (0.56, 1.28) | 0.70 (0.49, 1.01) | 0.73 (0.55, 0.98)* | 0.65 (0.53, 0.79)** | 0.87 (0.58, 1.31) | 0.73 (0.60, 0.88) | 1.44 (0.93, 2.22) | 0.99 (0.57, 1.69) |
| >4 | 0.62 (0.40, 0.98) | 0.29 (0.18, 0.48)** | 0.47 (0.34, 0.66)** | 0.38 (0.30, 0.48)** | 0.28 (0.15, 0.53)** | 0.51 (0.41, 0.64)** | 1.09 (0.69, 1.75) | 0.50 (0.26, 0.93)* |
| Unknown | 0.99 (0.67, 1.48) | 0.65 (0.45, 0.95)* | 0.71 (0.53, 0.96)* | 0.57 (0.47, 0.70)** | 0.63 (0.40, 1.01) | 0.61 (0.50, 0.75)** | 1.07 (0.67, 1.69) | 0.87 (0.50, 1.50) |
| *Procedure score* | | | | | | | | |
| 0 | Referent | Referent | Referent | Referent | Referent | Referent | Referent | Referent |
| 1 | 1.26 (0.91, 1.76) | 1.88 (1.33, 2.67)* | 1.63 (1.26, 2.10)* | 1.65 (1.38, 1.98)** | 1.38 (0.95, 2.01) | 1.61 (1.36, 1.91)** | 1.28 (0.94, 1.75) | 1.06 (0.67, 1.65) |
| 2 | 2.72 (1.79, 4.15)** | 3.90 (2.55, 5.96)* | 3.25 (2.37, 4.47)** | 3.21 (2.56, 4.01)** | 1.51 (0.89, 2.56) | 2.55 (2.06, 3.15)** | 1.64 (1.05, 2.56) | 2.98 (1.72, 5.16)** |
| ≥3 | 3.80 (1.88, 7.69)** | 5.07 (2.47, 10.41)** | 4.06 (2.34, 7.03)** | 4.68 (3.22, 6.80)** | 2.82 (1.11, 7.19)* | 3.15 (2.14, 4.63)** | 1.58 (0.63, 3.93) | 2.14 (0.65, 7.02) |

[1] Data only available from 2011–2012

[2] Data only available from 2010–2012

## Table 5

Model fit statistics.

| | | C-Statistic | Ability to distinguish | Pseudo-$R^2$ | AIC | LRT |
|---|---|---|---|---|---|---|
| Wound complications (n=2870) | Age | 0.537 | 7.4% | 0.0012 | 1419.243 | 3.4369 |
| | Functional status | 0.511 | 2.2% | 0.0008 | 1425.249 | 5.4310 |
| | Preoperative albumin | 0.561 | 12.2% | 0.0034 | 1413.036 | 9.6434 |
| | Procedure score | 0.593 | 18.6% | 0.0109 | 1391.343 | 31.3372 |
| | Combination of age, functional status, albumin | 0.588 | 17.6% | 0.0067 | 1413.329 | 19.3506 |
| | All four measures (age, functional status, albumin, procedure score) | 0.642 | 28.4% | 0.0169 | 1389.839 | 48.8411 |
| | Full model | 0.678 | 35.6% | 0.0252 | 1397.325 | 73.3545 |
| Severe complications (n=2870) | Age | 0.567 | 13.4% | 0.0038 | 1427.440 | 10.9687 |
| | Functional status | 0.533 | 6.6% | 0.0022 | 1417.753 | 20.6553 |
| | Preoperative albumin | 0.651 | 30.2% | 0.0199 | 1380.832 | 57.5768 |
| | Procedure score | 0.648 | 29.6% | 0.0218 | 1375.213 | 63.1950 |
| | Combination of age, functional status, albumin | 0.665 | 33% | 0.0266 | 1373.103 | 77.3050 |
| | All four measures (age, functional status, albumin, procedure score) | 0.720 | 44% | 0.0441 | 1326.896 | 129.5123 |
| | Full model | 0.743 | 48.6% | 0.0532 | 1331.600 | 156.8090 |
| Any complication (n=2870) | Age | 0.555 | 11% | 0.0046 | 2091.445 | 13.1221 |
| | Functional status | 0.520 | 4% | 0.0055 | 2088.809 | 15.7581 |
| | Preoperative albumin | 0.610 | 22% | 0.0173 | 2054.415 | 50.1513 |
| | Procedure score | 0.637 | 27.4% | 0.0320 | 2011.340 | 93.2270 |
| | Combination of age, functional status, albumin | 0.626 | 25.2% | 0.0238 | 2047.416 | 69.1509 |
| | All four measures (age, functional status, albumin, procedure score) | 0.688 | 37.6% | 0.0504 | 1974.189 | 148.3781 |
| | Full model | 0.702 | 40.4% | 0.0580 | 1983.202 | 171.3646 |
| Prolonged hospitalization (n=2870) | Age | 0.582 | 16.4% | 0.0164 | 3156.133 | 47.4187 |
| | Functional status | 0.526 | 5.2% | 0.0161 | 3157.011 | 46.5404 |
| | Preoperative albumin | 0.664 | 32.8% | 0.0718 | 2989.583 | 213.9682 |
| | Procedure score | 0.662 | 32.4% | 0.0808 | 2961.806 | 241.7456 |
| | Combination of age, functional status, albumin | 0.690 | 38% | 0.0911 | 2941.442 | 274.1096 |

| | | C-Statistic | Ability to distinguish | Pseudo-$R^2$ | AIC | LRT |
|---|---|---|---|---|---|---|
| | All four measures (age, functional status, albumin, procedure score) | 0.753 | 50.6% | 0.1540 | 2741.417 | 480.1349 |
| | Full model | 0.779 | 55.8% | 0.1810 | 2680.337 | 573.2142 |
| Non-routine discharge (n=1959) | Age | 0.712 | 42.4% | 0.0424 | 952.002 | 84.9319 |
| | Functional status | 0.549 | 9.8% | 0.0177 | 1001.914 | 35.0197 |
| | Preoperative albumin | 0.666 | 33.2% | 0.0250 | 987.309 | 49.6255 |
| | Procedure score | 0.578 | 15.6% | 0.0060 | 1025.146 | 11.7883 |
| | Combination of age, functional status, albumin | 0.777 | 55.4% | 0.0716 | 903.415 | 145.5188 |
| | All four measures (age, functional status, albumin, procedure score) | 0.785 | 57% | 0.0752 | 901.838 | 153.0959 |
| | Full model | 0.802 | 60.4% | 0.0877 | 893.031 | 179.5974 |
| Transfusion (n=2319) | Age | 0.556 | 11.2% | 0.0093 | 2943.943 | 21.7242 |
| | Functional status | 0.505 | 1% | 0.0021 | 2960.882 | 4.7846 |
| | Preoperative albumin | 0.626 | 25.2% | 0.0513 | 2843.558 | 122.1086 |
| | Procedure score | 0.657 | 31.4% | 0.0838 | 2762.649 | 203.0175 |
| | Combination of age, functional status, albumin | 0.642 | 28.4% | 0.0584 | 2838.119 | 139.5482 |
| | All four measures (age, functional status, albumin, procedure score) | 0.714 | 42.8% | 0.1234 | 2678.186 | 305.4804 |
| | Full model | 0.724 | 44.8% | 0.1372 | 2665.431 | 342.2354 |
| Non-routine discharge (n=2870) | Age | 0.711 | 42.2% | 0.0295 | 1064.521 | 85.8993 |
| | Functional status | 0.545 | 9% | 0.0087 | 1125.304 | 25.1159 |
| | Preoperative albumin | 0.655 | 31% | 0.0156 | 1105.310 | 45.1098 |
| | Procedure score | 0.592 | 18.4% | 0.0059 | 1133.306 | 17.1145 |
| | Combination of age, functional status, albumin | 0.767 | 53.4% | 0.0458 | 1027.978 | 134.4422 |
| | All four measures (age, functional status, albumin, procedure score) | 0.779 | 55.8% | 0.0497 | 1021.978 | 146.4418 |
| | Full model | 0.869 | 73.8% | 0.0980 | 904.377 | 296.0429 |
| Readmission (n=1959) | Age | 0.519 | 3.8% | 0.0005 | 1307.245 | 1.0269 |
| | Functional status | 0.503 | 0.6% | 0.0002 | 1305.856 | 0.4165 |
| | Preoperative albumin | 0.541 | 8.2% | 0.0027 | 1302.939 | 5.3328 |
| | Procedure score | 0.549 | 9.8% | 0.0033 | 1301.791 | 6.4815 |
| | Combination of age, functional status, albumin | 0.550 | 10% | 0.0033 | 1311.807 | 6.4652 |
| | All four measures (age, functional status, albumin, procedure score) | 0.572 | 14.4% | 0.0063 | 1311.936 | 12.3358 |

| | | C-Statistic | Ability to distinguish | Pseudo-$R^2$ | AIC | LRT |
|---|---|---|---|---|---|---|
| | Full model | 0.599 | 19.8% | 0.0110 | 1324.515 | 21.7572 |
| Reoperation (n=2870) | Age | 0.538 | 7.6% | 0.0007 | 906.815 | 1.9986 |
| | Functional status | 0.506 | 1.2% | 0.0003 | 907.995 | 0.8179 |
| | Preoperative albumin | 0.577 | 15.4 | 0.0028 | 900.725 | 8.0886 |
| | Procedure score | 0.574 | 14.8 | 0.0056 | 892.674 | 16.1394 |
| | Combination of age, functional status, albumin | 0.591 | 18.2% | 0.0038 | 909.918 | 10.8956 |
| | All four measures (age, functional status, albumin, procedure score) | 0.641 | 28.2% | 0.0090 | 900.887 | 25.9263 |
| | Full model | 0.691 | 38.2% | 0.0176 | 907.731 | 51.0820 |

Full model includes: age, race, ASA, BMI, albumin, preoperative functional status, year of diagnosis, and number of cytoreductive procedures. C-statistics measures discriminative power of the model. A value of 0.5 (null model) indicates that the model's predictions are no better than chance, whereas a value closed to 1 indicates that the model has a good prediction. Ability to distinguish is calculated from c-statistics (=((C-statistics − 0.5)/0.5)*100%). Higher Pseudo-$R^2$ indicates that the model explains more observed variation in the outcome. When only one variable is included in the model, the lower the AIC, the higher the importance of the variable in the model. The LRT compares the null model (no variables) to a model including one variable or one group of variables. Higher LRT indicates greater improvement in fit when the specified group of variables is included.