



## Perioperative blood transfusion in gynecologic oncology surgery: Analysis of the National Surgical Quality Improvement Program Database



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### HIGHLIGHTS

- 13.8% of gynecologic surgical patients received a perioperative blood transfusion.
- Transfusion is independently associated with increased perioperative morbidity.
- Transfusion increases risk of perioperative mortality and surgical site infections.

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### ABSTRACT

**Objective.** To use a large-scale multi-institutional dataset to quantify the prevalence of packed red blood cell transfusions and examine the associations between transfusion and perioperative outcomes in gynecologic cancer surgery.

**Methods.** The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) participant use file was queried for all gynecologic cancer cases between 2010 and 2012. Demographic, preoperative and intraoperative variables were compared between transfusion and non-transfusion groups using chi-squared, Fisher's exact and Wilcoxon rank-sum tests. The primary endpoint was 30-day composite morbidity. Secondary endpoints included composite surgical site infections, mortality and length of stay.

**Results.** A total of 8519 patients were analyzed, and 13.8% received a packed red blood cell transfusion. In the multivariate analysis, after adjusting for key clinical and perioperative factors, including preoperative anemia and case magnitude, transfusion was associated with higher composite morbidity (OR = 1.85, 95% CI 1.5–2.24), surgical site infections (OR 1.80, 95% CI 1.39–2.35), mortality (OR 3.38, 95% CI 1.80–6.36) and length of hospital stay (3.02 days v. 7.17 days,  $P < 0.001$ ).

**Conclusions.** Blood transfusions are associated with increased surgical wound infections, composite morbidity and mortality. Based on our analysis of the NSQIP database, transfusion practices in gynecologic cancer should be scrutinized. Examination of institutional practices and creation of transfusion guidelines for gynecologic malignancies could potentially result in better utilization of blood bank resources and clinical outcomes among patients.

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### Introduction

Blood is a precious, costly resource that is often over utilized and transfused with great variation in clinical practice. According to the US Department of Health and Human Services there were more than 13.5 million units of blood transfused in 2011 at an average

cost of \$225.42/unit [1]. Perioperative surgical transfusion rates in gynecologic oncology patients fluctuate greatly with some studies reporting rates as low as 3% [2] and others as high as 77% [3–5]. This wide variation in practice patterns may be attributed to vague clinical practice guidelines combined with conflicting data in cancer patients.

Several large randomized controlled trials have suggested that a more restrictive transfusion protocol in surgical and critically ill patients is associated with improved clinical outcomes [6–10]. Although there have been no randomized controlled trials in oncology patients, there is ample evidence in the colorectal cancer surgery literature to suggest that blood transfusions themselves are immunosuppressive and

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associated with increased rates of infection, perioperative morbidity, disease progression and mortality [11,12].

There is compelling evidence that questions the liberal use of blood transfusion in colorectal surgery and critically ill patients; however, uncertainties remain about the application of these data to gynecologic cancer patients. There are limited data examining the effects of blood transfusions on perioperative outcomes after gynecologic cancer surgery. Furthermore, to date, most of the studies in gynecologic cancer have been single-institution studies evaluating outcomes in a single disease site such as cervix or ovary.

Awareness of national blood transfusion practices in gynecologic oncology could potentially result in better utilization of blood bank resources and both short- and long-term clinical outcomes among patients. We hypothesized that blood transfusions are associated with increased morbidity in gynecologic oncology surgical patients. We used a large-scale multi-institutional dataset, the National Surgical Quality Improvement Program database, to quantify the prevalence of perioperative blood transfusion and examine the effect of transfusion on perioperative outcomes.

## Materials and methods

The American College of Surgeons National Surgical Quality Improvement Program (ASC-NSQIP) is a multi-institutional comprehensive database containing perioperative information on surgical patients. Trained risk-assessment nurses in participating hospitals collect preoperative patient characteristics, intraoperative data and 30-day morbidity and mortality. The specific methodology has been reported previously [13]. De-identified patient information is available to all participating institutions through the ASC-NSQIP participant use file (PUF).

The ASC-NSQIP PUF was queried for all gynecologic cases between 2010 and 2012 and limited to cases with ICD-9 codes associated with malignant gynecologic neoplasms (vulva, vagina, cervix, uterus, and ovary). CPT codes for which the transfusion rate was zero were excluded based on the findings by Bernard et al. [14]. Extreme outliers were excluded from the analysis which included patients with preoperative transfusion greater than 4 units, those undergoing emergency procedures, pelvic exenteration, or procedures with operative time less than 30 min.

A total of 8519 cases were included for analysis. The demographic data assessed included: age, body mass index (BMI), ethnicity (Hispanic and non-Hispanic) and race (white, black, other). Medical comorbidities and risk factors analyzed included: American Society of Anesthesiologists (ASA) class, presence of disseminated cancer, presence of ascites, receipt of neoadjuvant chemotherapy within 30 days of surgery, smoking, steroid use, hypertension requiring medication management, dyspnea, COPD, disease site (uterus, ovary, vagina/vulva, or cervix), preoperative bleeding disorders and more than 10% body weight loss in last 6 months. Perioperative factors evaluated included: preoperative labs (including hematocrit, INR, platelets and albumin), operating time, anesthesia time, procedure complexity, wound classification and procedure type. Procedure complexity was assessed by using total work relative value scales (WRVU), which has been previously shown to be an appropriate surrogate marker for surgical complexity [13]. Procedure type was defined as minimally invasive surgery (MIS) or open. Perioperative variables with less than 1% incidence were excluded.

Patients were divided into two groups: those who received a blood transfusion and those who did not receive a blood transfusion. The variable for transfusion includes those patients who received a transfusion in the operating room until up to 72 h postoperatively. The primary endpoint for the study was 30-day composite morbidity (based on the occurrence of 1 or more of the 20 adverse events defined by NSQIP, excluding transfusion, which are listed in Fig. 1). Secondary endpoints examined were: 30-day composite infectious morbidity (superficial,

deep or organ/space surgical site infections), the 20 adverse events defined by NSQIP, mortality, and length of stay.

Summary statistics were used to describe demographic, preoperative and intraoperative variables. Chi-squared and Fisher's exact tests were used to test for differences between those who received a blood transfusion and those who did not receive a blood transfusion for categorical variables, and the Wilcoxon rank-sum test was used to compare medians between groups for continuous variables.

Univariate logistic regression was used to model the logit of the probability of composite morbidity as a function of whether or not a patient received a transfusion and several other potential prognostic factors. A saturated model including all factors with a  $P < 0.20$  was built and backward elimination was used in a multivariate analysis to construct a parsimonious model, removing factors one at a time until all remaining factors remained statistically significant. Preoperative hematocrit was retained as a continuous variable in all models. Adjusted odds ratios and corresponding 95% confidence intervals for each factor remaining in the model are reported.  $P < 0.05$  was considered statistically significant. This modeling strategy was repeated for composite surgical site infections (SSI). However, since there were only 53 events for mortality, a forward selection strategy was used to build a multivariate model. The model began with transfusion (yes/no), and then the factor with the smallest  $P$  was added and the model was refit. All factors with  $P < 0.05$  were retained and this process was repeated until no remaining factors could enter the model. This strategy avoided overfitting the model. All analyses were performed using STATA™ 13.0 for Macintosh (StatCorp LP, College Station, Texas). The study was approved by The University of Texas MD Anderson Cancer Center Institutional Review Board.

## Results

We identified 8906 patients with the diagnosis of gynecologic malignancy in the NSQIP database. Three hundred eighty-seven patients were excluded for the following reasons: emergency case ( $n = 61$ ), exenterative procedure ( $n = 88$ ), preoperative transfusion more than 4 units ( $n = 79$ ), operative time less than 30 min ( $n = 74$ ) and CPT codes with transfusion rate of zero ( $n = 85$ ). Of the 8519 patients who met our inclusion criteria, 1178 or 13.8% (95% CI 13.1%–14.6%) received a blood transfusion within 72 h of surgery.

Procedures were grouped according to primary CPT code and organ system (Table 1). Laparoscopy was the most common procedure performed ( $n = 3916$ ), followed by open abdominal hysterectomy ( $n = 2483$ ) then laparotomy for tumor reductive surgery ( $n = 1773$ ). Laparotomy associated with a tumor reductive surgery had the highest propensity for blood transfusion with 35.08% of patients receiving at least one transfusion, followed by vaginectomy (23.53%) and laparotomy for adnexal surgery (18.18%). Laparoscopy was associated with the lowest likelihood of having a transfusion (2.32%).

Comparison of the demographics and preoperative characteristics of patients who received a blood transfusion and those who did not is displayed in Table 2. Compared to those patients who did not receive a transfusion, patients who were transfused were more likely to be older, thinner, non-white, have a higher ASA class, and have disseminated cancer, dyspnea, ovarian cancer, and a bleeding disorder. Comparison of preoperative laboratory variables between patients who received a blood transfusion and those who did not is displayed in Table 3. Compared to those patients who did not receive a transfusion, patients who were transfused were more likely to have a lower preoperative hematocrit, and a preoperative albumin less than 3 ( $P < 0.001$  for all). While our primary interest was to evaluate the association of morbidity with transfusion use, we considered the above factors in our multivariate analysis of morbidity in an effort to account for potential bias in differences between those patients who did and did not receive transfusions. Importantly, we accounted for

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