Effect of Perioperative Blood Transfusion on Mortality for Major Urologic Malignancies

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Abstract

We used the Surveillance, Epidemiology, and End Results-Medicare data set from 1992 to 2009 to identify patients who underwent surgery for prostate, bladder, or renal cancer. Univariate and multivariate models were used to evaluate the association of perioperative blood transfusion (PBT) with cancer-specific mortality (CSM) and all-cause mortality (ACM). PBT was associated with increased CSM and ACM for prostate and kidney but not bladder cancer.

Introduction: Patients who undergo surgical treatment for malignancy often receive perioperative blood transfusion (PBT). We examined the association between PBT and mortality in patients who received surgical treatment of prostate, bladder, and kidney cancer. **Materials and Methods:** Using the Surveillance, Epidemiology, and End Results-Medicare data set from 1992-2009, we identified 28,854 men with prostate cancer, 5462 patients with bladder cancer, and 14,379 patients with renal cell carcinoma who underwent radical prostatectomy (RP), radical cystectomy (RC), or radical (RN) or partial nephrectomy (PN) as primary therapy. Univariate and multivariate models were used to evaluate the association of PBT with cancer-specific mortality (CSM) and all-cause mortality (ACM). **Results:** The rate of PBT in bladder and kidney cancer have been increasing over time, and PBT in prostate cancer steadily increased and peaked in 2002 and declined afterward. The median follow-up for the RP, RC, and RN/PN cohorts were 70 months, 21 months, and 39 months, respectively. In the RP cohort, PBT was associated with greater CSM (hazard ratio [HR], 1.609; 95% confidence interval [CI], 1.235-2.097; $P = .0004$) and ACM (HR, 1.121; 95% CI, 1.006-1.251; $P = .0394$). In the RC cohort, PBT was not associated with greater CSM (HR, 1.047; 95% CI, 0.917-1.195; $P = .4962$) or ACM (HR, 1.095; 95% CI, 0.998-1.200; $P = .0547$). In the nephrectomy cohort, PBT was associated with greater CSM (HR, 1.365; 95% CI, 1.167-1.597; $P = .0001$) and ACM (HR, 1.402; 1.273-1.544; $P < .0001$). **Conclusion:** PBT was associated with increased CSM and ACM for prostate and kidney cancer in a multivariate model. Although these data do not identify a causative relationship between PBT and mortality, efforts made to limit PBT in patients who undergo urologic cancer surgery can yield long-term survival benefits.

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Introduction

Surgical resection remains a critical component of optimal treatment for many solid organ tumors. The risks and ultimate outcomes of these operations are based on several factors including the disease stage, tumor grade, patient comorbidities, and perioperative course. The effects of perioperative blood transfusion (PBT) on morbidity, mortality, and recurrence of disease after cancer surgery have previously been studied in several malignancies. Studies in colorectal, esophageal, and hepatocellular cancer patients have demonstrated increased risk of adverse outcomes for patients who received PBT.[1-4] Although several immune-related effects of transfusion have been hypothesized as an explanation for these findings,[5] the exact etiology of increased cancer recurrence and decreased survival in association with PBT remains unclear.

Previous studies have also evaluated the effect of PBT in the realm of urologic malignancies. For prostate cancer, although the literature has conflicting reports, most recent data failed to note an effect of PBT on biochemical failure, progression, or survival in prostate cancer patients.[6-8] Conversely, several recent studies have reported worse outcomes in bladder cancer patients who have received PBT with radical cystectomy (RC).[9-11] Studies evaluating the association of PBT and outcomes in renal cell carcinoma (RCC) have identified

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conflicting results.[12-14] Hence, controversy remains regarding the effect of PBT on recurrence and survival in patients who undergo major extirpative surgery for urologic tumors. Many of the previous studies are subject to restrictive single-institution populations, were smaller in sample size, and may have been subject to institutional biases and norms regarding triggers for transfusion. The population trend in the incidence of PBT is also not known.

The objective of this study was to evaluate the association between receipt of PBT in patients who underwent surgery for major urologic malignancies and survival rates in a large population-based data set that allowed us to examine this question in the context of customary practice in the community at large.

Materials and Methods

Data

The Surveillance, Epidemiology, and End Results (SEER)-Medicare linked file, from 1992 through 2009, was used to complete this study. This file reports information related to demographic characteristics, pathology, treatment, and death for patients with a cancer diagnosis and includes information on covered health services claims of Medicare-eligible patients. Information on the linkage of these databases can be found elsewhere.[15] The tumor registries represent approximately 26% of the population of the United States.[16]

Cohort Selection

Cancer-specific sites were identified by topographic codes and histological codes. We identified 43,677 men with adenocarcinoma of the prostate, 7251 patients with urothelial cell carcinoma of the bladder, and 19,014 with RCC. Those diagnosed at autopsy/nursing homes, patients enrolled at health management organizations; patients diagnosed in Louisiana in 2005, and those lacking socioeconomic information were excluded. We included patients who underwent radical prostatectomy (RP) for prostate cancer, RC for bladder cancer, and radical nephrectomy (RN) or partial nephrectomy (PN) for RCC. A list of current procedural terminology (CPT) codes used to identify patients who underwent each procedure is reported in Appendix A. This process yielded 28,854 patients with prostate cancer, 5462 patients with bladder cancer, and 14,379 patients with RCC who were treated with extirpative surgery during the study period.

Variables

The data collected from the SEER file included demographic information (age in 5-year increments), race/ethnicity, sex, and region of residence (SEER registry), tumor stage, histological grade, and type of procedure. Data related to income and education were extracted and evaluated in quartiles. We used the Klabunde's modification[17] of the Deyo method[18] to calculate the Charlson score for each patient with the use of Medicare claims in the 12 months before the diagnosis of cancer.[19,20] Treatments were identified by CPT, International Classification of Disease ninth revision (ICD-9) procedure codes. Surgeons were identified by their unique provider identification number (UPIN) and surgeon volume was determined by the number of patient-level procedures associated with a UPIN. Hospital volume was determined by the number of site-specific cancer-directed surgeries performed in each hospital. Physicians and hospitals were classified as low or high volume based on the total number of procedures performed. PBT was defined as transfusion of red blood cells during and up to 7 days after cancer-directed surgery (see Appendix A for codes used). The decision to use this definition, rather than including preoperative transfusion, is consistent with most reports in the literature. Transfusion during surgery and in the postoperative period is believed to be the true driver of any effect on outcomes and represents most of all transfusions around the time of surgery. Only 5% of all transfusions were preoperative in our data set, rendering the effect from such transfusions negligible.

Analysis

Univariate descriptive statistics and the trend of PBT over the study period were evaluated for each malignancy. Unadjusted associations between transfused and nontransfused patients were examined using χ^2. We performed separate logistic regression using generalized estimating equation methods that adjusted for clustering and to control for confounders and determine the predictors of PBT in each cohort. To reduce the effect of selection bias on blood transfusion, separate propensity-based Cox proportional hazard models were used to determine the adjusted effect of covariates, determined a priori, on the risks of cancer-specific mortality (CSM) and all-cause mortality (ACM). Weighted Kaplan–Meier analysis was also completed. See Appendix B for more details on propensity score modeling. Analysis was completed using SAS statistical software, version 9.3 (SAS Institute Inc, Cary, NC). A P value $< .05$ was considered significant.

Results

Prostate Cohort

The median age of the RP cohort was 69 (interquartile range [IQR], 67-72) years. The median postoperative follow-up was 70 (IQR, 33-119) months. Details of clinicopathologic demographic characteristics are shown in Table 1. Neither tumor stage nor grade was statistically different between those who received PBT, and those who did not. Approximately 7% received PBT. The frequency of PBT increased with age ($P < .0038$). Patients with greater comorbidity had higher rates of PBT ($P < .0001$). There was no significant variation in the receipt of transfusion by geographic region, clinical tumor stage, or histological grade. Figure 1 shows the trend of PBT over time, which demonstrates an increase up to 8.93% in 2002 and subsequent decrease to a rate of 5.94%, which was close to levels seen in 1992.

Table 2 shows the odds of receipt of PBT using a logistic regression model. The likelihood of receipt of PBT increased significantly with age at diagnosis ($P < .005$). Men with greater baseline comorbidity were more likely to receive PBT ($P < .0001$). The odds of receipt of PBT did not vary significantly by tumor stage or histologic grade. Patients who underwent RP by high volume surgeons or who underwent robotic RP were less likely to receive a transfusion ($P < .0001$). Hospital volume did not seem to affect the likelihood of receipt of PBT ($P = .0602$).

Table 3 shows the CSM and ACM in a propensity-based Cox regression. The likelihood of CSM and ACM increased with age compared with men 66-69 years of age ($P < .0001$). Greater hazard ratios (HRs) were observed for CSM (HR, 2.725; 95% confidence