



Original article

Restrictive transfusion in radical cystectomy is safe

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Abstract

Introduction and objective: Perioperative blood transfusion (PBT) is commonplace in radical cystectomy (RC) and has been linked to poorer oncologic outcomes. Limiting PBT in this largely elderly and comorbid population has not been studied. Herein, we first investigate the safety of a restrictive transfusion protocol (RTP) in patients undergoing RC for urothelial carcinoma and then compare oncologic outcomes between patients who did and did not receive PBT.

Methods: Outcomes for 173 consecutive patients meeting inclusion criteria undergoing RC for urothelial carcinoma from April 2010 to June 2014 by a single surgeon employing RTP were analyzed from an institutional review board–approved, prospectively collected database. Pairwise matching to a cohort undergoing RC during an earlier era of more liberal PBT was performed, and 90-day outcomes were compared.

Results: Median follow-up for the RTP cohort was 3.1 years (range: 0–5.1 y). Median age was 70 years (range: 38–93 y). Forty-six patients (26.6%) received PBT. Eighty-seven matched pairs were generated from RTP cohort and liberal era where PBT rate was 94%. There were no differences in 90-day complication rates, mortality, or readmission rates ($P > 0.05$). In the RTP cohort, patients who underwent PBT had higher estimated blood loss (500 vs. 350, $P = 0.001$), lower baseline hematocrit (28.9 vs. 33.3, $P = 0.005$), and similar operative time (5.8 vs. 5.3 h, $P = 0.01$) and length of stay (5.5 vs. 5, $P = 0.07$). At discharge and 3-week follow-up, there was no difference in hematocrit ($P > 0.05$). In the no-PBT group, 90-day (65.6% vs. 86.7%, $P = 0.007$) and high-grade (15.6% vs. 34.8%, $P = 0.003$) complication rates were lower. On multivariable analysis, predictors of PBT were age (odds ratio [OR] = 1.06, 95% CI [1.01–1.11]), Charlson comorbidity index ≥ 2 (OR = 2.68, CI [1.09–7.04]), neoadjuvant chemotherapy (OR = 3.74, CI [1.46–10.19]), $\geq pT3$ (OR = 5.5, CI [2.33–13.73]), baseline hematocrit (OR = 0.95, CI [0.87–1.00]), and estimated blood loss (OR = 1.001, CI [1–1.003]). PBT was associated with lower recurrence-free survival (hazard ratio = 2.16; CI [1.13–41.12]; $P = 0.02$) and overall survival (hazard ratio = 2.25; CI [1.25–4.88]; $P = 0.01$).

Conclusions: The use of RTP in RC is safe. PBT was associated with poorer recurrence-free survival and overall survival independent of clinicopathologic characteristics. © 2017 Elsevier Inc. All rights reserved.

Keywords: Bladder; Carcinoma, Urothelial; Radical cystectomy; Preoperative transfusion; Blood transfusion

1. Introduction

Perioperative blood transfusion (PBT) is a costly intervention with clinical as well as economic consequences [1,2]. In patients undergoing radical cystectomy (RC) for urothelial cancer (UC) of the bladder, PBT has been linked to worse oncologic outcomes; a risk that correlated to the number of units received [3–5].

Traditionally, open RC has been associated with a significant intraoperative blood loss and a correspondingly

high rate of PBT [6]. The RC patient population is largely elderly patients with significant comorbidities, and the clinician may be reasonably concerned about the risk of withholding transfusion in this setting. The issue of determining when PBT is needed and which patients will benefit is the topic of much debate, with newer literature disputing the benefits of liberal PBT even in patients with cardiac disease [7]. To date, consistent preoperative predictors for patients who will go on to require PBT after RC have not been identified, and the safety of restrictive transfusion protocols (RTP) in this setting has not been assessed [5].

In this study, we first compared perioperative outcomes in patients undergoing RC by a single surgeon employing an

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RTP to those from an earlier period at the same institution where PBT use was liberal to see if RTP conferred higher complications. We then examined patients who received PBT and those who did not within the RTP cohort to identify predictors of PBT and compare oncologic outcomes.

2. Materials and methods

All subjects were part of an institutional review board–approved database. Data were obtained from paper and electronic records, deidentified, and organized in a secure database. All anomalies triggered another review by 2 independent investigators.

From April 2010 to June 2014, 223 consecutive patients underwent RC by a single surgeon employing a restrictive approach to PBT. Of these, 173 patients met inclusion criteria (bladder primary UC, intent to cure, not undergoing total pelvic exenteration, and available follow-up data). No other clinical factors were applied as exclusion criteria. PBT was defined as allogeneic blood cell transfusion during RC or hospital stay. The RTP was adopted from current American College of Cardiology/American Heart Association (ACC/AHA) and American Society of Anesthesiologists (ASA) guidelines and was defined as follows: preoperatively, patients <75 years old with no significant cardiac disease should have hemoglobin (Hgb) > 8 mg/dl, and >9 mg/dl if older than 75 or with cardiac history. For these groups, postoperative Hgb is maintained at more than 7 or 8 mg/dl [8,9]. When transfusion is required, 1 unit packed red blood cells is given and then clinical and laboratory reassessment is performed.

This cohort was matched to a database of 714 patients undergoing RC at the same institution from 2003 to 2010: a period of liberal transfusion use. Pairwise matching by age, sex, pathologic subgroup, ASA score, type of urinary diversion, and neoadjuvant chemotherapy status was performed, and 87 matched pairs were generated.

All cases were performed in an open approach using an institutionally standardized technique that includes an extended pelvic lymph node dissection as previously described [10]. A bipolar tissue sealant device (LigaSure), sealant agent (Tisseel), and hemostatic agent (FloSeal) were used in an attempt to minimize intraoperative and postoperative blood loss.

Statistical analysis was performed using SAS version 9.4. Multivariable analyses using logistic and Cox regression modeling were performed.

3. Results

3.1. Characteristics of RTP cohort as a whole

A total of 173 consecutive patients underwent open RC with extended pelvic lymph node dissection during the study period. Median length of follow-up was 3.1 years (range: 0–5.1 y). Median age was 70 years (range: 38–93 y). Median

body mass index was 26.7 (15.9–41.7). Overall, 46 patients (26.7%) received PBT, who received a median of 2 units transfused (1–12). Further, 134 patients (77.5%) underwent continent diversion of which 121 (69.9%) were orthotopic. For the cohort as a whole, median operative time was 5.4 hours (2.7–10.7) and estimated blood loss (EBL) was 400 ml (75–1,800).

3.2. Comparing perioperative outcomes in restrictive and liberal transfusion groups

The RTP cohort was compared to the liberal transfusion era where PBT rate was 94% ($n = 87$ pairs). There were no differences in preoperative characteristics between liberal and restrictive groups, except for baseline hematocrit that was higher at 37.6 vs. 30.9 ($P < 0.001$). EBL was higher at 1,240 vs. 458 ml ($P < 0.001$). By 3 weeks postoperatively, there was no difference in hematocrit between groups. Overall, 90-day complication rates were similar with 50 patients (57.5%) and 53 patients (60.9%) in liberal and restrictive eras, respectively ($P = 0.76$), experiencing complications (Table 3). Mean number of complications per patient was 1.4 in liberal era and 1.3 in restrictive era ($P = 0.81$). There was no difference in the number of complications within each grade ($P = 0.38$), nor was there a difference seen when complications were grouped into low- vs. high-grade complications ($P = 0.88$). Infection and renal insufficiency (including all types of postoperative renal insufficiency) were the most common subtypes of complications seen in both eras. Cardiac complications were seen in 10.3% and 9.2% of patients in liberal and restrictive eras, respectively, which was not statistically significantly different ($P = 1.00$). Most cardiac complications in either era were postoperative arrhythmia. Readmission rates within 90 days were similar at 23% and 21.8% ($P = 1.00$).

3.3. Comparing outcomes in PBT and no-PBT patients in the RTP cohort

Hematocrits' trends were analyzed from the following time points: baseline (preoperatively), immediately postoperatively, upon discharge, and at 3-week follow-up. There were differences in hematocrit between those who did not receive PBT and those who did, respectively, at baseline (39.6 [25.9–49.6] vs. 34.9 [25.5–46], $P = 0.001$) and immediately postoperatively (28.8 [19.3–42.8] vs. 26.7 [20.4–35.9], $P = 0.2$), but not by the time of discharge or at follow-up ($P > 0.05$) (Table 1).

On univariable analysis, patients who were transfused had higher median EBL at 500 ml (75–1,800) vs. 350 ml (100–1,600), $P = 0.001$, and lower baseline hematocrit as mentioned but showed no clinically important difference in operative time (5.8 vs. 5.3 h) or length of stay (LOS) (5.5 vs. 5 d, $P = 0.07$). Patients undergoing orthotopic diversion were less likely to receive transfusion (21.5% vs.

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