Clinical utility of routine postoperative serial hemoglobin measurements in patients undergoing radical cystectomy for urothelial carcinoma

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ABSTRACT

Introduction: Routine measurements of serum hemoglobin (sHgb) are common after abdominal surgery; however, prolonged measurements may be associated with patient anxiety, increased costs, and longer hospitalization without clinical benefit. The objective of this study was to determine the utility of routine sHgb measurements after radical cystectomy (RC) and factors associated with transfusion of packed red blood cell (pRBC) beyond postoperative day (POD) 2.

Methods: We retrospectively reviewed patients who underwent RC between 2009 and 2019 at a single academic tertiary care center. The number of sHgb measurements for each patient was examined and pRBC transfusion rates were calculated. Multivariable logistic regression was used to determine factors associated with transfusion beyond POD 2.

Results: The median number of sHgb measurements per patient during admission was 9 (interquartile range [IQR] 7,25). Overall, 69/240 (28.7%) patients received a postoperative transfusion, including 46/240 (19.2%) patients receiving a transfusion beyond POD 2. Among

KEY MESSAGES

- Transfusion of packed red blood cells beyond postoperative day 2 following radical cystectomy is common.
- Factors associated with delayed transfusion were found to be age, length of stay in hospital and serum hemoglobin on postoperative day 2.
- Patients with a serum hemoglobin of ≥100 g/L on postoperative day 2 are at low risk of requiring subsequent transfusions.
- Discontinuing routine serum hemoglobin measurements in these patients may serve to decreased patient anxiety, costs, and delays in hospital discharge

patients with a sHgb ≥100 g/L on POD 2, 7/85 (8.2%) went on to receive a transfusion beyond this day compared with 39/155 (25.2%) patients with sHgb <100 g/L. On multivariable analysis, risk factors associated with pRBC transfusion beyond POD 2 included older age, lower sHgb on POD 2, and longer length of stay in hospital.
Conclusions: Transfusion of PRBCs beyond POD2 was found to be common; however, patients with sHgb ≥100 g/L on POD 2 were at low risk of requiring subsequent transfusion. Discontinuing further routine sHgb checks in these patients may serve to decrease patient anxiety, healthcare costs, and delays in hospital discharge.

INTRODUCTION

Urothelial carcinoma (UC) of the bladder is a common and often fatal disease. Among solid organ tumours in the United States (US), it is the ninth leading cause of cancer related mortality, accounting for almost 18,000 deaths in the year 2020 alone.[1] Radical cystectomy (RC) with urinary diversion is the gold standard treatment for muscle invasive UC of the bladder. RC, however, is associated with significant morbidity with roughly 50% of patients experiencing a complication within 30 days of surgery.[2] Anemia requiring transfusion of packed red blood cells (pRBC) is among the most common postoperative complications encountered and occurs in 22-59% of patients.[2-4]

While in hospital, patients are commonly subjected to routine daily blood work encompassing a range of measurements including serum hemoglobin (sHgb). The timing surrounding discontinuation of routine bloodwork differs between centres and patients depending on their postoperative day (POD), clinical status and overall progression. Little evidence exists regarding optimal timing of discontinuation. The utility of routine bloodwork in the postoperative period has been questioned across a range of surgical specialties including urology.[5-7] Eliminating routine blood work in select patients has the potential to decrease health care costs, reduce patient anxiety and discomfort and limit unnecessary delays in discharge. The primary objective of this study was to examine pRBC transfusion rates and timing of these transfusions following RC to determine the clinical utility of routine serial postoperative sHgb measurements. Our secondary objective was to identify patient factors associated with "delayed transfusion," defined as transfusion beyond POD 2.

METHODS

Following institutional review board approval, we conducted a retrospective chart review of patients undergoing RC for UC at a single Canadian academic tertiary care centre between 2009 and 2019. Patients for which benign disease or non-urothelial malignancy was the primary indication for surgery were excluded. There were no further inclusion or exclusion criteria.

Patient demographics were collected along with a range of preoperative, intraoperative and postoperative data. The primary outcomes of interest were the number of sHgb measurements performed on POD 0, 1, 2, and beyond day 2 as well as the total number of postoperative sHgb measurements performed on each patient. The secondary outcome of interest was clinical and patient factors associated with delayed transfusion.

Descriptive statistics were used to characterize our patient population and calculate transfusion rates. Univariable and multivariable logistic regressions were performed to investigate the association between patient characteristics and receipt of delayed transfusion. P-value of <0.05 was used to denote statistical significance for all. Odds ratios (OR) and 95% confidence intervals (CI) were recorded. Statistical analysis was performed using SPSS version 26.0.

RESULTS

We identified 240 patients who underwent open RC for UC by 6 different surgeons in the 10-year study period. Patients were predominately male (81.2%) with a median age of 70 years. The majority were American Society of Anesthesiologists (ASA) class 2 (61%) and underwent ileal conduit urinary diversion (85%). Overall, 66.1% of patients experienced a complication during their initial postoperative hospital admission. Most complications (72.7%) were Clavien-Dindo Grade I or II in nature. Median length of stay (LOS) in hospital was 10 days. Table 1 summarizes demographic and perioperative data for the entire cohort.

In total, 3317 postoperative sHgb measurements were done in our study population. The median number of postoperative sHgb measurements per patient was 9 (IQR 7, 15). Transfusion of pRBCs occurred in 40.8% of patients including 23.3% intraoperatively and 29.2% during the initial postoperative hospital admission. A significant minority (n=46, 19.2%) of patients were transfused beyond POD 2. Table 2 outlines rates and timing of transfusion of pRBCs.
Among patients with a sHgb level $\geq$ 100 g/L on POD 2, only 7/85 (8.2%) went on to receive a delayed transfusion. Comparatively, 39/155 (25.2%) patients with a sHgb < 100 g/L on POD 2 went on to receive a delayed transfusion. Patients with a sHgb level $\geq$ 100 g/L on POD 2 who went on to receive a delayed transfusion all experienced complicated postoperative courses as outlined in Table 3.

Multivariable logistic regression identified that age, LOS, and sHgb on POD 2 were associated with delayed transfusion. Table 4 shows the full multivariable model.

DISCUSSION

Herein we examined pRBC transfusion rates, timing of pRBC transfusion, and variables associated with delayed transfusion in patients undergoing RC for UC at our institution. We found that patents with a sHgb $\geq$ 100 g/L on POD 2 were at low risk of receiving a transfusion of pRBCs beyond this date. Variables associated with delayed transfusion were found to be age, LOS and sHgb on POD 2.

Eliminating unnecessary routine postoperative bloodwork has been studied across several surgical specialties. Chamsy et al. found routine postoperative sHgb measurement to be of no clinical benefit following elective laparoscopic hysterectomy for benign disease.[6] Their analysis estimated potential cost savings of $2,804,662 per year in the US by eliminating routine postoperative sHgb testing in this population. Mostello et al. examined the utility of routine postoperative sHgb measurements in patients undergoing primary total joint arthroplasty.[7] They found a transfusion rate of 0% in patients with a sHgb > 125 g/L preoperatively and > 100 g/L on POD 1. Eliminating subsequent measurements in these patients would have resulted in an overall reduction of 56% in sHgb measurements after POD 1 and significant savings. Furthermore, limiting routine bloodwork to those at increased risk for complication has been shown to be an effective and safe strategy. By limiting investigations to at risk patients, Nathan et al. demonstrated a reduction in routine postoperative bloodwork from 100% to 27% in patients undergoing robot assisted laparoscopic radical prostatectomy.[7] Benefits in their study included reduction in bloodwork related discharge delays from 6% to 0% with no missed postoperative complications during their study period.

To our knowledge this is the first study to examine the clinical utility of routine postoperative sHgb following RC. In this same population, we have previously shown prolonged postoperative serum creatinine monitoring to be of little clinical utility.[8] In our study population a total of 3317 sHgb measurements were done. The median number of measurements per patient was 9, closely mirroring the median LOS of 10 days. This suggests most patients had routine bloodwork drawn daily without discrimination. We identified a group of patients in which transfusion of pRBCs beyond POD 2 was uncommon. In patients with a sHgb of $\geq$ 100 g/L on POD 2 (n=85) delayed transfusion occurred in only 8.2% (n=7) of cases. Comparably, delayed transfusion occurred in 25.2% (n=39) of patients with a sHgb < 100 g/L on POD 2 (n=155). Patients with a sHgb $\geq$ 100 g/L on POD 2 who went on to receive a delayed transfusion all experienced significant complications of Clavien-Dindo Grade III or greater in nature (Table 3). Median LOS in this group was 37 days vs. the 10 days observed in our entire cohort. Among patients with a sHgb $\geq$ 100 g/L on POD 2 who did not get transfused (n=78), an additional 603 sHgb measurements were performed.

Transfusion of pRBCs is common following RC and has been associated with increased morbidity in the postoperative period, surgical site infection, re-admission and increased risk of cancer recurrence and mortality.[9,10] Many factors have been associated with perioperative transfusion including age, female gender, higher ASA class, preoperative anemia, cardiovascular co-morbidities and continent urinary diversion.[10,11] Our study is unique in that we identified specific timing of transfusion in the postoperative period. We found an overall transfusion rate of 40.8%, similar to that reported in the literature. Surprisingly, greater numbers of patients were transfused beyond POD 2 (19.2%) then POD 0, 1 and 2 combined (17.5%). While this was an unexpected finding it likely reflects the morbidity of the procedure and the fact that many

complications arise outside the initial 48 hours postoperatively. Volume of phlebotomy has been shown to be associated with changes in sHgb in patients admitted to an internal medicine service and to a lesser extent, routine daily bloodwork in our population may have contributed to anemia and subsequent delayed transfusion.[12] On multivariate logistic regression analysis, the only factors associated with transfusion beyond POD 2 were age, LOS and sHgb on POD 2. The association with age likely reflects patient frailty and co-morbidities although ASA class was not found to be significant. LOS supports the notion that patients receiving delayed transfusions are those not following a routine postoperative course.

Limitations to our study include its retrospective nature and single centre design. Additionally, we looked at sHgb and its relation to postoperative transfusion in isolation without looking at other components of the complete blood count such as white blood cell count (WBC). While the authors contend that an elevated WBC in an otherwise asymptomatic patient following an expected postoperative course is of minimal clinical utility, further research is required in this area. Finally, our study includes patients who underwent open RC exclusively. The applicability of our results to those undergoing minimally invasive RC is unknown.

CONCLUSIONS

Patients undergoing RC for UC are at a high risk of pRBC transfusion. Delayed transfusions are common in this patient population and are associated with increasing age, LOS in hospital and sHgb on POD 2. However, RC patients with a sHgb of $\geq$ 100 g/L on POD 2 are at low risk of requiring subsequent transfusion of pRBCs. Eliminating ongoing routine sHgb measurement in these patients may result in decreased patient anxiety, costs, and delays in hospital discharge.

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Figures and Tables

Table 1. Demographic and perioperative data	
Demographic (n=240)	
Gender	M 81.2%, F 18.8%
Median age (years)	70 (IQR 62, 76)
Median BMI	27.3 (IQR 24.4, 30.6)
Neoadjuvant chemotherapy	37.7%
ASA classification	1 – 3.4%
	2 – 61.0%
	3 – 34.7%
	4 – 1.7%
	5 – 0.0%
Median preoperative sHgb (g/L)	128 (IQR 111, 144)
Median OR time (minutes)	178.5 (IQR 150, 226)
Median EBL (mls)	500 (IQR 400, 700)
Urinary diversion	Ileal conduit 85.0%
	Neobladder 10.8%
	Cutaneous ureterostomies 3.75%
	Other 0.45%
Median LOS (days)	10 (IQR 8, 14)
Clavien-Dindo complication rates	Grade I – 17.2%
	Grade II – 31.0%
	Grade III – 10.5%
	Grade IV – 5.9%
	Grade V – 1.7%
	Any complication – 66.3%

ASA: American Society of Anesthesiologists; BMI: body mass index; EBL: estimated blood loss; IQR: interquartile range; LOS: length of stay; OR: operating room; sHgb: serum hemoglobin.

Table 2. Transfusion rates of pRBCs and timing following RC	
Time of transfusion	
Intraoperative	23.3%
Postoperative	29.2%
POD 0	5.8%
POD 1	7.5%
POD 2	6.7%
POD > 2	19.2%
Overall	40.8%

POD: postoperative day; pRBC: packed red blood cells; RC: radical cystectomy.

Table 3. Postoperative course of patients with sHgb ≥100 on POD 2 who received a delayed transfusion of pRBCs

	LOS (days)	**Number of pRBC units transfused beyond POD 2**	**Clavien-Dindo complication grade**	**Nature of complications**	**Comments**
Patient #1	37	2	IV	1. Aspiration pneumonia 2. Urosepsis	Therapeutic anticoagulation for history of VTE
Patient #2	31	2	III	1. Acute PE 2. Percutaneous drainage of intra-abdominal collection 3. Prolonged ileus	Therapeutic anticoagulation initiated in hospital, metastatic disease
Patient #3	13	3	III	1. Acute PE 2. GI bleed	Therapeutic anticoagulation initiated in hospital
Patient #4	243	8	IV	1. Multiple fascial dehiscences 2. Enterocutaneous fistula 3. Intra-abdominal sepsis 4. VTE	Therapeutic anticoagulation initiated in hospital, total of 5 separate OR take backs including eventual mesh reconstruction of abdominal wall with skin grafting
Patient #5	49	1	III	1. Mechanical SBO	OR take back for lysis of adhesions, single unit transfused perioperatively

Patient #6	21	5	IV	1. Unrecognized rectal injury 2. Intra-abdominal sepsis	OR take back for washout and Hartmann's procedure, 5 units transfused perioperatively
Patient #7	151	4	V	1. Urine leak 2. Prolonged ileus 3. Recurrent episodes of hypoxic respiratory failure 4. Death	Urine leak managed with percutaneous drain and nephrostomy tubes, death from respiratory failure secondary to recurrent aspiration

GI: gastrointestinal; LOS: length of stay; OR: operating room; PE: pulmonary embolism; POD: postoperative day; pRBC: packed red blood cells; RC: radical cystectomy; SBO: small bowel obstruction, sHgb: serum hemoglobin; VTE: venous thromboembolism.

Table 4. Multivariable logistic regression examining factors associated with transfusion of pRBCs beyond POD 2

Variable	**OR (95% CI)**	**p**
Age	1.05 (1.00–1.11)	0.072
LOS	1.17 (1.10–1.25)	<0.0001
sHgb on POD 2	0.89 (0.85–0.94)	<0.0001
Neoadjuvant chemotherapy	1.97 (0.70–5.59)	0.201
Intraoperative tranexamic acid	0.29 (0.05–1.71)	0.171
Change in sHgb from POD 1 to 2	0.98 (0.93–1.03)	0.390
Estimated blood loss	1.00 (0.99–1.01)	0.469
Preoperative sHgb	1.01 (0.98–1.04)	0.623
Sex (ref: male)	2.69 (0.71–10.18)	0.146
BMI	1.01 (0.99–1.02)	0.238

BMI: body mass index; CI: confidence interval; LOS: length of stay; OR: odds ratio; POD: postoperative day; pRBC: packed red blood cells; sHgb: serum hemoglobin.