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Original article

Effect of blood transfusions on oncological outcomes of surgically treated localized renal cell csarcinoma

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Abstract

Objective: To assess the associations between perioperative allogeneic blood transfusions (ABTs) and recurrence, overall and renal cell carcinoma (RCC)-specific survival in patients undergoing surgical treatment for clinically localized disease.

Materials and methods: We performed a retrospective review of 1,056 consecutive patients undergoing surgical treatment (radical or partial nephrectomy) for clinically localized RCC between 2000 to 2010. Demographic (age, race, and sex) clinical (preoperative hemoglobin and hematocrit, type of surgery [partial or radical nephrectomy]), and pathological (T and N stages, RCC histotype, grade) data were compared between patients receiving perioperative (intraoperative or postoperative) blood transfusions and those who are not. Distant and local recurrence-free survival, overall survival, RCC-specific survival were recorded and Kaplan-Meier survival curves as well as multivariable proportional regression models adjusted for clinical and pathological characteristics were produced.

Results: On multivariable analyses adjusted for clinical and pathological characteristics, the receipt of ABTs was associated with lower recurrence-free (HR = 1.86, $P = 0.002$), overall (HR = 1.83, $P = 0.016$), and RCC-specific survival (HR = 2.12, $P = 0.031$). The negative effect of ABTs was apparent for distant (HR = 2.24, $P < 0.001$) but not local recurrences (HR = 0.78, $P = 0.643$). Limitations include retrospective nature and lack of uniform criteria for blood transfusion during the study period.

Conclusions: In this study, perioperative ABTs were independently associated with worse oncological outcomes in patients with clinically localized RCC. Receipt of ABT was associated with roughly a 2-fold increase in the hazard of metastatic progression, all-cause and RCC-specific mortality. Further research is needed on the mechanisms of transfusion-induced immunomodulation, alternative transfusion protocols and methods for autologous blood transfusion and recovery.

Keywords: Renal cell carcinoma; Blood transfusion; Survival

1. Introduction

Allogeneic blood transfusions (ABT) have immunomodulatory effects mediated by a variety of factors, including immunologically active white blood cells remaining in transfusion units, their soluble mediators, and soluble HLA peptides of the donor [1]. Clinically, these immunomodulatory effects translate into increased incidence of postoperative infections, reactivation of latent viruses as well as increased risk of recurrence in select malignancies [1].

In surgical oncology, the deleterious effects of ABTs have been shown for colorectal and several other cancers [2,3]. Conversely, in genitourinary oncology, only limited data exist evaluating the effect of ABTs on surgical and oncological outcomes. A recent study associated perioperative transfusions with increased risk of bladder cancer recurrence and mortality following radical cystectomy [4]. In kidney cancer, Margulis et al. [5] included receipt of blood transfusions as a prognostic variable in their nomogram for predicting survival after cytoreductive nephrectomy in metastatic renal cell carcinoma (RCC).In addition, Park et al. and Linder et al. assessed the association between blood transfusions and oncological outcomes for RCC. However, Linder et al. only considered distant metastasis

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as recurrence and Park et al., included T3 and T4 disease that may have introduced bias [6,7].

The aim of this study was to comprehensively assess the effect of ABTs on recurrence (distant and local), overall and RCC-specific survival in patients treated for clinically localized RCC.

2. Materials and methods

After approval from the Institutional Review Board, we retrospectively reviewed the records of adult patients undergoing surgical treatment for clinically localized renal masses between 2000 and 2010.

Patients undergoing either partial or radical nephrectomy were included. We excluded patients with metastatic disease at presentation, those with syndromes associated with RCC (e.g., Von Hippel Lindau and Birt Hogg Dube′) as well as those with pathological findings other than RCC.

We retrieved demographic (age, race, and sex) clinical (preoperative hemoglobin and hematocrit, type of surgery [partial or radical nephrectomy]), and pathological (T and N stages, RCC histotype, grade) data and identified patients receiving perioperative (intraoperative or during the postoperative hospitalization period) blood transfusions. Only ABTs of packed red blood cells (ABT) were considered for the purpose of this study and the number of units was recorded. The number of units transfused was categorized

Table 1
Patient characteristics and comparison between the groups

Variable	Overall	No ABT	ABT	*P* value
Number	1,056	883 (84%)	173 (16%)	
Age, y	61 (52–68)	60 (51–67)	65 (57–72)	<0.001
Sex				0.967
Male	654 (62%)	548 (62%)	106 (61%)	
Female	402 (38%)	335 (38%)	67 (39%)	
Race				0.963
White	737 (70%)	615 (70%)	122 (71%)	
Black	271 (26%)	228 (26%)	43 (25%)	
Other	48 (5%)	40 (5%)	8 (5%)	
BMI, kg/m^2	29.6 (26.1–33.9)	29.5 (26.2–33.8)	29.6 (25.7–34.8)	0.805
CCI	1 (0–3)	1 (0–3)	2 (0–3)	<0.001
Hematocrit, %	41 (38–44)	42 (39–45)	37 (33–40)	<0.001
Hemoglobin, mg/dl	13.7 (12.2–15.8)	13.9 (1.6–15.0)	12.1 (10.6–13.4)	<0.001
Anemia[a]	127 (12.4%)	69 (8.1%)	58 (35%)	<0.001
Surgery				0.090
Partial nephrectomy	632 (60%)	365 (41%)	59 (34%)	
Radical nephrectomy	424 (40%)	518 (59%)	114(66%)	
Surgical approach				<0.001
Open	715 (68%)	565 (64%)	150 (87%)	
MIS	341 (32%)	318 (36%)	23 (13%)	
Tumor size, cm	4.1 (2.8–6.9)	3.9 (2.7–6.0)	6.2 (4.0–9.8)	<0.001
EBL, ml	300 (125–600)	200 (100–450)	1,000 (500–2,000)	<0.001
RCC subtype				0.331
Clear cell	782 (74%)	646 (73%)	136 (79%)	
Papillary	212 (20%)	184 (21%)	28 (16%)	
Other	62 (6%)	53 (6%)	9 (5%)	
Nuclear grade				<0.001
1	212 (20%)	183 (21%)	29 (17%)	
2	614 (58%)	537 (61%)	77 (45%)	
3	175 (17%)	134 (15%)	41 (24%)	
4	51 (5%)	25 (3%)	26 (15%)	
Pathologic stage				<0.001
T1	764 (72%)	681 (77%)	83 (48%)	
T2	126 (12%)	98 (11%)	28 (16%)	
T3	150 (14%)	94 (11%)	56 (32%)	
T4	16 (2%)	10 (1%)	6 (3%)	
Nodal stage				<0.001
Nx	865 (82%)	752 (85%)	113 (65%)	
N0	160 (15%)	116 (13%)	44 (25%)	
N+	31 (3%)	15 (2%)	16 (9%)	

EBL = estimated blood loss; MIS = minimally-invasive surgery (laparoscopic, robot-assisted).
[a]Hemoglobin <12 g/dl for males and <10 for females.