




Perioperative Transfusions for Gastroesophageal Cancers: Risk Factors and Short- and Long-Term Outcomes

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Abstract

Background Perioperative blood transfusions have been associated with increased morbidity and poorer oncologic outcomes for numerous surgical procedures. However, this issue is understudied among patients with gastroesophageal malignancies. The objective was to clarify the risk factors and impact of perioperative transfusions on quality of life and surgical and oncologic outcomes among patients undergoing gastric and esophageal cancer surgery.

Methods Patients undergoing curative-intent resections for gastroesophageal cancers between 2010 and 2018 were included. Perioperative blood transfusion was defined as any transfusion within 24 h pre-operatively, during surgery, or the primary post-operative hospitalization period. Patient and tumor characteristics, surgical and oncological outcomes, and quality of life were compared.

Results A total of 435 patients were included. Perioperative transfusions occurred in 184 (42%). Anemia, blood loss, female sex, open surgical approach, and operative time emerged as independent risk factors for transfusions. Factors found to be independently associated with overall survival were neoadjuvant therapy, tumor size and stage, major complications, and mortality. Transfusions did not independently impact overall survival, disease-free survival, or quality of life.

Conclusions Perioperative transfusions did not impact oncologic outcomes or quality of life among patients undergoing curative-intent surgery for gastroesophageal cancers.

Keywords Esophagus · Gastric · Outcomes · Quality of life · Transfusions

Introduction

Gastroesophageal cancer patients are at high risk of anemia due to a multitude of cancer- and treatment-related factors¹. Anemia is often treated with red cell (pRBC) transfusions in this population, especially in the perioperative period for those

undergoing gastroesophagectomy². While necessary to preserve life during or after major surgery, transfusions have been associated with increased morbidity, worse oncologic outcomes, and decreased quality of life (QoL) in studies that evaluated patients with other cancers^{3–5}.

Since transfusions have been associated with increased cancer recurrence and risk of developing new tumors^{3,4,6–12}, some question the value of perioperative transfusions in cancer patients^{1,8,13–17}. The negative effects of transfusion are thought to be due to transfusion-related immunomodulation; allogenic red blood cell transfusion reduces the activity of natural killer cells and T lymphocytes^{4,6,7,9,10}. These cells are required to prevent dissemination of circulating and quiescent cancer cells and for providing resistance to infections^{6,18}. However, the effect of perioperative transfusions among gastroesophageal cancer patients is understudied and not defined clearly.

Therefore, the purpose of this study was to assess the impact of perioperative pRBC transfusions on operative, oncologic, and QoL outcomes among patients with gastroesophageal cancers.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11605-020-04845-7>.

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Methodology

Study Subjects

Patients who underwent treatment for gastroesophageal cancer from January 2010 to December 2018 were identified from a prospectively collected database. Patients undergoing curative-intent surgery for gastric and esophageal cancers were included while palliative, prophylactic, and benign resections; rare cancers (non-adenocarcinoma or squamous cell carcinoma) and other synchronous and/or prior cancers were excluded.

Definition of Perioperative Transfusions

Patients were classified as having been transfused in the perioperative period if they received red cell transfusions 24 h pre-operatively, during surgery, or within the post-operative hospitalization period of their cancer resection^{9,13,15,19–23}.

Data Collection and Classification

The primary outcomes were cumulative overall and disease-free survival. Secondary outcomes included patient and tumor characteristics, operative outcomes, complications, and quality of life determined at baseline and at every follow-up visit. All data were collected prospectively and extracted from paper and electronic medical records.

Age-adjusted Charlson comorbidity index (CCI) was used to categorize comorbidities and age²⁴. Node-negative and T1–2 stage tumors were classified as early-stage cancer²⁵ while any node-positive disease and T3–4 were classified as locally advanced cancer^{26,27}. Anemia was categorized according to the World Health Organization's (WHO's) cut-offs: mild (110 g/L to normal), moderate (80 g/L to 110 g/L), and severe anemia (less than 80 g/L)²⁸. All tumors were classified according to the American Joint Committee on Cancer (AJCC) eighth edition^{29,30}. Post-operative complications were classified using the Clavien-Dindo score (CDS)³¹. Death certificates and Quebec cancer registry data were used to determine mortality. Functional Assessment of Cancer Therapy-Esophageal (FACT-E) questionnaires administered at every outpatient clinic appointment were used to determine QoL scores³².

Statistical Analysis

Data were analyzed using Mann-Whitney *U*, Fisher-Exact, Kaplan-Meier, log-rank, and χ^2 tests. Multiple logistic regression was used for determining independent risk factors for transfusions with the model being built using statistically significant factors identified on univariate analysis and clinically relevant parameters. Cox proportional hazards regression

model was employed to determine variables independently predictive of overall (OS) and disease-free survival (DFS). Prism 8.0 by GraphPad and SAS 9.4 by SAS Institute were utilized for statistical analysis. Data are presented as median interquartile range. A *p* value of less than 0.05 determined statistical significance.

Results

Of 766 gastroesophageal resections performed between 2010 and 2018, 446 met inclusion criteria. Among those, 11 (2%) were excluded due to lack of transfusion data leaving 435 patients included in the final analysis, of which 184 (42%) received transfusions perioperatively.

Patients were older and had more severe comorbidities in the transfusion group. Adenocarcinoma predominated in both groups and clinical stage was higher in the transfusion group (stage III-IV: pRBC: 106 (57%), no pRBC: 111 (45%); *p* = 0.002). Coagulation parameters, rates of neoadjuvant therapy (pRBC 124 (67%), no pRBC 160 (64%); *p* = 0.570), and quantity of transfusions before surgery (pRBC 0–2 units, no pRBC 0–1 units; *p* = 0.342) did not vary among groups. Anemia was more prevalent in the transfusion group at all timepoints: hemoglobin at diagnosis (pRBC 124 108–138 g/L, no pRBC 137 119–148 g/L; *p* < 0.001), pre-operatively (pRBC 109 99–120 g/L, no pRBC 126 115–138 g/L; *p* < 0.001), and on day of surgery (pRBC 102 89–113 g/L, no pRBC 121 115–132 g/L; *p* < 0.001). Patient characteristics are presented in Table 1.

Transfusions were more prevalent among those who had surgery using the open approach (Table 2). Duration of surgery was comparable among groups while estimated blood loss (EBL) was higher in the transfusion group (pRBC 500 250–750 mL, no pRBC 250 150–400 mL; *p* < 0.001). Transfused patients received 1–2 pRBC units per patient intra-operatively and 1–2 units post-operatively, with 38 (43%) of post-operative transfusions occurring in patients who had also received pRBC transfusions during surgery. The rate of transfusions decreased from 50 to 40% over the study period (Fig. 1). Severe post-operative complications (Clavien-Dindo 3–4) (pRBC 56 (30%), no pRBC 37 (15%); *p* < 0.001) and 30-day mortality (pRBC 14 (8%), no pRBC 2 (1%); *p* < 0.001) were higher in the transfusion group.

Tumors were larger in the transfusion group (pRBC 4.3 ± 3.2 cm, no pRBC 3.3 ± 2.4 cm; *p* = 0.003) and had more lymph node (LN) metastasis (pRBC 2–7 nodes, no pRBC 1–3 nodes; *p* = 0.031). Total number of LNs retrieved and lymphovascular and perineural invasion were comparable among groups. Pathological stage, positive margins, and rates of pathologic complete response were similar between groups. However, tumors were more invasive (T4 pRBC 34 (18%), no

Table 1 Patient characteristics by group

	pRBC (<i>n</i> = 184)	No pRBC (<i>n</i> = 251)	<i>p</i> value
Male sex, <i>n</i> (%)	134 (73)	200 (80)	0.119
Age (years), Mdn [IQR]	68 [60–76]	65 [59–73]	0.010*
BMI (kg/m ²), $\bar{x} \pm \sigma_x$	25 ± 5	26 ± 5	0.003*
CCI, <i>n</i> (%)			0.008*
Mild (1–2)	4 (2)	16 (6)	
Moderate (3–4)	72 (39)	121 (48)	
Severe (≥ 5)	108 (59)	114 (45)	
Tumor location, <i>n</i> (%)			0.008*
GEJ	111 (60)	159 (63)	
Stomach	47 (26)	78 (31)	
Esophagus	26 (14)	14 (6)	
Histology, <i>n</i> (%)			0.026*
Adenocarcinoma	158 (86)	232 (92)	
Squamous cell carcinoma	26 (14)	19 (8)	
Clinical stage, <i>n</i> (%)			0.002*
0	0 (0)	3 (1)	
I	17 (9)	40 (16)	
II	23 (13)	55 (22)	
III	100 (54)	107 (43)	
IVA	6 (3)	4 (2)	
Tumor extension <i>n</i> (%)			< 0.001*
Tis	0 (0)	3 (1)	
T1	10 (5)	31 (12)	
T2	13 (7)	37 (15)	
T3	124 (67)	148 (59)	
T4	11 (6)	5 (2)	
Node status, <i>n</i> (%)			0.006*
N0	72 (39)	130 (52)	
N+	89 (48)	91 (36)	
Distant metastasis, <i>n</i> (%)			0.701
M0	164 (89)	225 (90)	
Mx	4	7	
Neoadjuvant therapy, <i>n</i> (%)	124 (67)	160 (64)	0.570
Chemotherapy	99 (54)	135 (54)	
Chemoradiotherapy	21 (11)	22 (9)	
Immunotherapy	2 (1)	2 (1)	
Hematology at diagnosis, Mdn [IQR]			
Hemoglobin (g/L)	124 [108–138]	137 [119–148]	< 0.001*
Hematocrit (vol%)	0.369 [0.330–0.412]	0.410 [0.362–0.440]	< 0.001*
pRBC during workup, Mdn [IQR]	0 [0–2]	0 [0–1]	0.342
Pre-operative hematology, Mdn [IQR]			
Hemoglobin (g/L)	109 [99–120]	126 [115–138]	< 0.001*
Hematocrit (vol%)	0.327 [0.298–0.365]	0.378 [0.345–0.410]	< 0.001*
PT (seconds)	12.5 [11.5–13.4]	12.5 [11.5–13.3]	0.764
INR	1.01 [0.96–1.06]	1.00 [0.95–1.06]	0.271
aPTT (seconds)	26.9 [24.6–33.7]	28.4 [25.1–34.7]	0.222
Hematology on day of surgery, Mdn [IQR]			
Hemoglobin (g/L)	102 [89–113]	121 [115–132]	< 0.001*
Hematocrit (vol%)	0.302 [0.272–0.334]	0.366 [0.343–0.390]	< 0.001*
Pre-operative pRBC units, Mdn [IQR]	0 [0–0]	0 [0–0]	0.631
ERAS pathway, <i>n</i> (%)	161 (88)	228 (91)	0.807

aPTT, activated partial thromboplastin time; *BMI*, body mass index; *CCI*, age-adjusted Charlson comorbidity index; *ERAS*, enhanced recovery after surgery; *GE*, gastroesophageal; *GEJ*, gastroesophageal junction; *INR*, international normalized ratio; *IQR*, interquartile range; *Mdn*, median; *pRBC*, packed red blood cell transfusion; *PT*, prothrombin time; *Tis*, carcinoma in situ; *vol%*, volume percentage; \bar{x} , mean; σ_x , standard deviation

* Statistically significant value

pRBC 18 (7%); $p < 0.001$) and had a higher LN status in the transfusion group. Oncological outcomes are presented in Table 3. On multivariate analysis, independent risk factors

for receiving perioperative pRBC transfusions (Table 4) were female sex, moderate to severe anemia on day of surgery, EBL above 400 mL, open approach, and prolonged operative time.

Table 2 Operative outcomes by study group

	pRBC	No pRBC	<i>p</i> value
Approach, <i>n</i> (%)			< 0.001*
Open	156 (85)	167 (66)	
Minimally invasive	28 (15)	84 (33)	
Procedure, <i>n</i> (%)			0.692
Ivor-Lewis esophagectomy	76 (41)	111 (44)	
Subtotal gastrectomy	26 (14)	58 (23)	
LTA esophago-gastrectomy or extended total gastrectomy	25 (14)	30 (12)	
Total gastrectomy	24 (13)	18 (7)	
McKeown esophagectomy	13 (7)	22 (9)	
Transhiatal distal esophagectomy	11 (6)	10 (4)	
Complex esophagectomy ^a	9 (5)	2 (1)	
Duration of surgery (min), Mdn [IQR]	220 [180–270]	210 [163–259]	0.057
Blood loss (mL), Mdn [IQR]	500 [250–750]	250 [150–400]	< 0.001*
Intra-operative pRBC, Mdn [IQR]	1 [0–2]	0 [0–0]	< 0.001*
Post-operative pRBC, Mdn [IQR]	1 [0–2]	0 [0–0]	< 0.001*
Perioperative pRBC, Mdn [IQR]	2 [2–4]	0 [0–0]	< 0.001*
Length of stay (days), Mdn [IQR]	10 [7–18]	7 [6–8]	< 0.001*
30-day ER visits, <i>n</i> (%)	24 (13)	29 (12)	0.628
30-day readmissions, <i>n</i> (%)	16 (9)	29 (12)	0.381
30-day complications, <i>n</i> (%)			< 0.001*
CDS 0	22 (12)	112 (45)	
CDS 1–2	92 (50)	99 (39)	
CDS 3–4	56 (30)	37 (15)	
CDS 5	14 (8)	2 (1)	

CDS, Clavien-Dindo score; ER, emergency room; IQR, interquartile range; LTA, left thoracoabdominal; Mdn, median; pRBC, packed red blood cell transfusion

* Statistically significant value

^a Laryngopharyngoesophagectomy, modified radical neck dissections, interposition flaps

Kaplan-Meier survival curves for DFS and OS are depicted in Fig. 2. Those who did not receive pRBC transfusions had higher DFS and OS on univariate analysis. Figure 3 demonstrates an inverse relationship between survival and quantity of pRBC transfused for both DFS and OS.

Cox proportional hazard analysis for DFS (Table 5) demonstrated the following factors to independently influence DFS: neoadjuvant therapy and pathological stage negatively impacted DFS. Table 6 depicts factors that were independently associated with OS: neoadjuvant therapy, major complications

Fig. 1 Percentage of patients receiving packed red cell transfusions in the interval beginning 24 h pre-operatively to the end of their post-operative stay over the study period

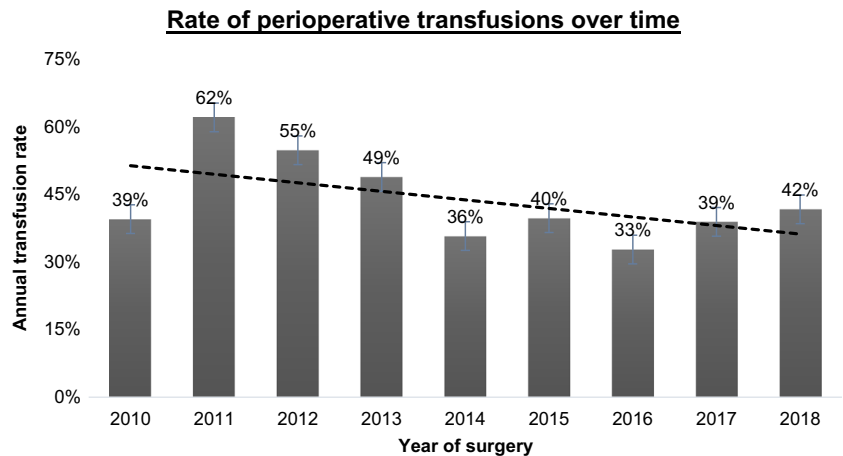


Table 3 Oncologic outcomes by group

	pRBC	No pRBC	<i>p</i> value
Tumor size ^a (cm), $\bar{x} \pm \sigma_X$	4.3 ± 3.2	3.3 ± 2.4	0.003*
LN _s , median [IQR]			
Positive	2 [0–7]	1 [0–3]	0.031*
Total removed	33 [24–46]	31 [23–41]	0.114
Lymphovascular invasion, <i>n</i> (%)	97 (53)	124 (49)	0.775
Perineural invasion, <i>n</i> (%)	94 (51)	118 (47)	0.648
AJCC stage, <i>n</i> (%)			0.180
0	2 (1)	5 (2)	
I	46 (25)	81 (32)	
II	31 (17)	46 (18)	
III	83 (45)	102 (41)	
IVA	22 (12)	17 (7)	
Tumor extension, <i>n</i> (%)			< 0.001*
T0	9 (5)	15 (6)	
Tis	1 (0.5)	3 (1)	
T1	27 (15)	66 (26)	
T2	23 (13)	44 (18)	
T3	90 (49)	105 (42)	
T4	34 (18)	18 (7)	
Node status, <i>n</i> (%)			< 0.001*
N0	78 (42)	104 (41)	
N1	25 (14)	66 (26)	
N2	36 (20)	51 (20)	
N3	45 (24)	30 (12)	
M0, <i>n</i> (%)	184 (100)	251 (100)	0.900
Pathologic complete response ^b , <i>n</i> (%)	8 (6)	12 (8)	0.856
Positive margin, <i>n</i> (%)	1 (1)	4 (2)	0.319

AJCC, American Joint Committee on Cancer; IQR, interquartile range; LN, lymph node; M, distant metastasis; N, LN metastasis; pRBC, packed red blood cell transfusion; T, tumor extension; \bar{x} , mean; σ_X , standard deviation

* Statistically significant value

^a Greatest dimension of tumor as measured by pathologist

^b Only applies to patients with neoadjuvant therapy

(Clavien-Dindo score 3–5), pathological stage, and tumor size above 3 cm negatively impacted OS. When controlling for other factors, transfusions were not found to independently impact DFS or OS.

Patient-reported QoL scores from FACT-E questionnaires are presented in Fig. 4. Quality of life was similar

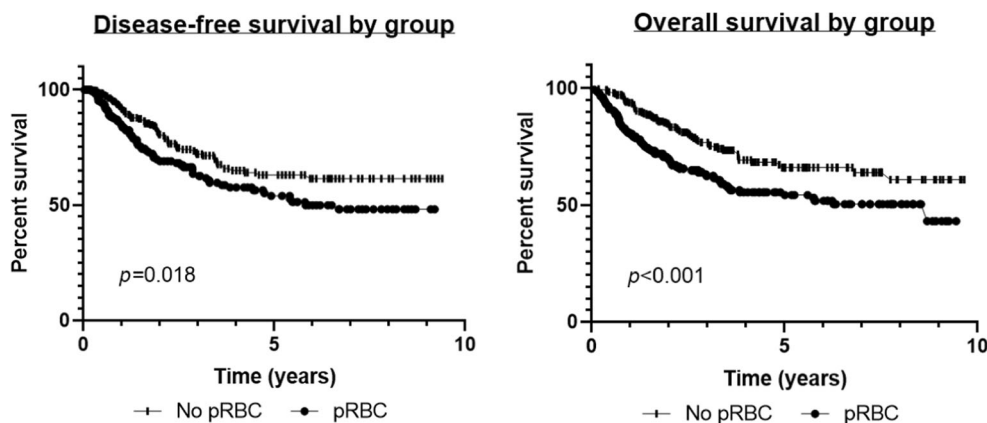
between groups at all timepoints from diagnosis to follow-up 3 years post-operatively. Trends in overall quality of life show a decrease in the early post-operative period and rebound to higher than pre-operative levels after 3 months post-operatively, but these differences did not reach statistical significance.

Table 4 Multivariate analysis for prognostic factors of perioperative red cell transfusion

Risk factor	Odds ratio	95% confidence interval	<i>p</i> value
Age > 60 years	1.105	[0.408–2.989]	0.845
Anemia (moderate-severe)	6.208	[3.342–11.530]	< 0.001*
Blood loss > 400 mL	4.878	[2.657–8.954]	< 0.001*
Body mass index	1.225	[0.321–4.684]	0.766
Comorbidities (severe)	9.954	[0.829–119]	0.070
Female sex	2.827	[1.425–5.608]	0.003*
Gastrectomy versus esophagectomy	1.445	[0.673–3.100]	0.345
Locally advanced cancer	1.594	[0.598–4.244]	0.351
Neoadjuvant therapy	0.749	[0.326–1.720]	0.496
Open versus minimally invasive approach	4.048	[1.724–9.504]	0.001*
Operative time (minutes)	1.008	[1.002–1.014]	0.005*

* Statistically significant value

Fig. 2 Kaplan-Meier survival curves for disease-free and overall survival

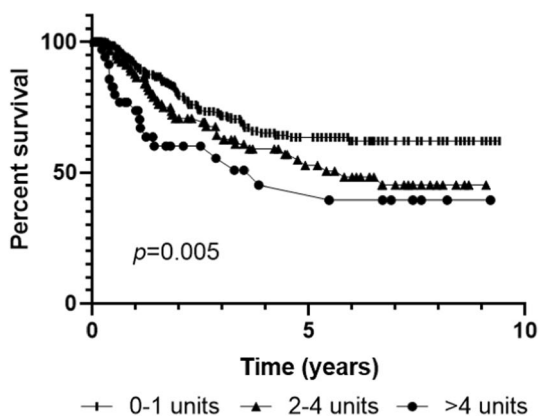


Discussion

This study demonstrated that perioperative pRBC transfusions can be administered safely for patients undergoing curative-intent surgery for gastroesophageal cancers without impacting QoL or surgical and oncological outcomes. Independent risk factors for transfusion in this series were anemia, intra-

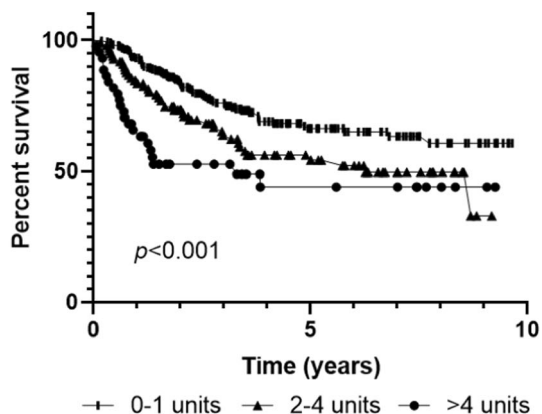
operative blood loss, open approach surgery, prolonged operative time, and female sex. Importantly, transfusions did not negatively impact surgical outcomes and long-term survival. The results of this study are significant as perioperative transfusions have been associated with poorer oncologic and surgical outcomes for other cancers, but this has not been studied in gastroesophageal cancer patients.

Disease-free survival by quantity of transfusion



The relationship between perioperative blood transfusions and survival is controversial. Many studies have shown a significant deleterious effect on survival related to perioperative transfusions while some demonstrated similarity^{6,22}. Often, these studies have been limited by small sample sizes and use of univariate analysis alone, making interpretation of the true impact of transfusions challenging^{22,23,33,34}. Furthermore, large database studies are limited by a lack of granularity of data^{15,22,33}. Several studies reporting worse long-term oncologic outcomes in transfused patients do not include some significant parameters in their multivariate model such as intra-operative blood loss and pre-operative hemoglobin level. When multivariate modeling has adjusted for such important covariates, a deleterious impact of transfusions has not been demonstrated^{18,23,35,36}. These articles demonstrate that transfusions, even though they tend to be associated with decreased survival in some studies, do not independently impact survival when confounding variables are incorporated into multivariate analysis, which is in keeping with the findings we report in this analysis.

Overall survival by quantity of transfusion



Disease-free survival was lower in the transfused group in our univariate analysis, which mirrors other studies^{13,22}. However, this significant difference disappeared on multivariate analysis when covariates were taken into consideration, indicating that transfusions are a confounding factor more than a prognostic indicator²¹. Neoadjuvant therapy and pathological tumor stage independently influenced DFS^{6,13,15,21,37,38}. Neoadjuvant therapy has a positive correlation with DFS since it is used for locally advanced cancers to improve local tumor control. According to our results and those reported by others, age, sex, comorbidities, complications, tumor size, and approach did not influence DFS independently^{6,39,40}. Our

Fig. 3 Kaplan-Meier survival curves grouped by quantity of transfusions for disease-free and overall survival

Table 5 Cox proportional hazard analysis for disease-free survival

	Hazard ratio	95% confidence interval	<i>p</i> value
Age 60+ years	1.199	[0.650–2.215]	0.561
Comorbidities (severe)	0.964	[0.369–2.521]	0.941
Female sex	1.259	[0.835–1.899]	0.271
Gastrectomy versus esophagectomy	1.162	[0.771–1.753]	0.473
Major complications and death	1.414	[0.929–2.153]	0.106
Neoadjuvant therapy	1.672	[1.064–2.628]	0.026*
Open versus minimally invasive approach	1.174	[0.705–1.956]	0.537
Overall tumor stage ^a			
II	3.227	[1.477–7.050]	0.003*
III	7.687	[3.933–15.023]	< 0.001*
IVA	9.647	[4.271–21.791]	< 0.001*
Packed red blood cell transfusion ^b	1.397	[0.948–2.057]	0.091
Tumor size > 3 cm	1.223	[0.838–1.787]	0.297

* Statistically significant value

^a Stage I used as reference for pathological stage^b No transfusions used as reference

results demonstrate that perioperative transfusions do not independently impact disease-free survival and that multivariate analysis is necessary to determine whether transfusions impact survival.

Overall survival in this series was significantly longer on univariate analysis among non-transfused patients, implying transfusions may deleteriously impact survival ^{16,22,34,35}. However, we demonstrated that this difference disappears with multivariate analysis where transfusion does not influence OS when confounders are considered ³⁵. Contrary to our findings, transfusions remained an independent prognostic factor for OS in some studies ^{13,34}. This could be attributed to the variables used in the multivariate Cox regression

analysis, as these studies did not include some clinically important covariates such as complications and tumor size. The benefit of this single-center review of prospectively followed patients is the depth of data available, allowing for analysis of possible confounding variables related to outcomes. Our results showed that, as expected, stage, tumor size, complications, and mortality impact OS while transfusions alone do not.

Despite the differences in tumor stage, comorbidities approach, and complications observed among transfused and non-transfused patients in this cohort, QoL at all timepoints was similar among groups. We observed a trend towards improved QoL after neoadjuvant therapy and surgery, which can

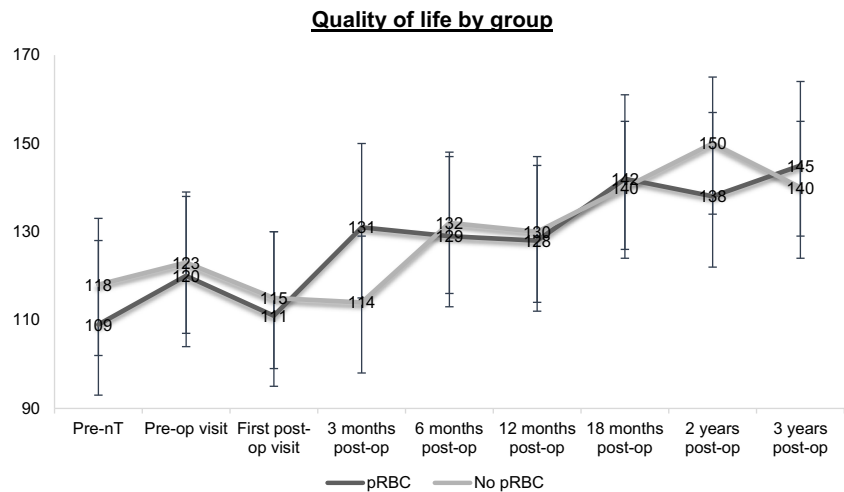
Table 6 Cox proportional hazard analysis for overall survival

	Hazard ratio	95% confidence interval	<i>p</i> value
Age 60+ years	1.433	[0.808–2.539]	0.218
Comorbidities (severe)	1.483	[0.529–4.158]	0.454
Female sex	1.162	[0.768–1.759]	0.478
Gastrectomy versus esophagectomy	0.905	[0.597–1.371]	0.638
Major complications and death	2.355	[1.624–3.415]	< 0.001*
Neoadjuvant therapy	1.768	[1.101–2.841]	0.019
Open versus minimally invasive approach	1.382	[0.807–2.368]	0.239
Overall tumor stage ^a			
II	1.481	[0.786–2.791]	0.224
III	2.591	[1.566–4.287]	< 0.001*
IVA	3.307	[1.721–6.355]	< 0.001*
Packed red blood cell transfusion ^b	1.222	[0.843–1.771]	0.289
Tumor size > 3 cm	1.711	[1.168–2.507]	0.006*

* Statistically significant value

^a Stage I used as reference for pathological stage^b No transfusions used as reference

Fig. 4 Quality of life scores from the Functional Assessment of Cancer Therapy–Esophageal questionnaire. nT, neoadjuvant therapy; post-op, post-operative



be attributed to dysphagia relief following commencement of treatment. While the differences in QoL at various timepoints did not reach statistical significance in this series, this is likely because gastric and esophageal cancer patients were grouped together in the analysis. Our group has previously demonstrated significant improvements in long-term QoL from baseline in upper gastrointestinal cancer patients⁴¹. Importantly, no differences in QoL were observed at any timepoint between transfused and non-transfused patients in this cohort.

Our results indicate that moderate to severe anemia, intra-operative blood loss, increased operative time, and female sex are independent risk factors for perioperative transfusion on multivariate analysis, as has been reported^{14, 22, 36, 42, 43}. Two benchmark studies showed that women tend to have a higher transfusion rate and volume, which can be explained by clinicians applying the same absolute transfusion thresholds irrespective of sex even though the WHO's anemia cut-offs for women are lower⁴⁴. In addition, no cut-off values or transfusion guidelines exist specifically for post-menopausal women. Consequently, female surgical patients tend to receive transfusions more often than men⁴⁴ and may explain why female sex emerged as an independent risk factor for transfusion in this series.

Limitations of this study include the retrospective nature of the data analysis. Nevertheless, the large patient cohort strengthens the validity of our findings. Additionally, this work was carried out in a single center, limiting the generalizability of our findings. Although neoadjuvant therapy protocols for esophageal and gastric cancer have evolved greatly over the study period, our center has been treating gastric and esophageal adenocarcinomas (the majority of patients in this study) with taxane-based triplet therapy (docetaxel, cisplatin, and 5-fluorouracil) since 2007⁴⁵, making this cohort relatively homogenous in this respect despite the lengthy study interval. Administration of adjuvant therapy was not evaluated, which could be a confounder for some variables such as quality of life and long-term survival. In addition, selection bias

was present as the decision to transfuse is subjective and some practitioners may have been more liberal with transfusions than others. Although the overall rate of perioperative transfusions in this cohort is high (46%), intra-operative transfusion rates (24%) were in line with globally reported standards. Our data also show transfusions were given more liberally in the earlier years of the study. Indeed, a trend towards decreasing overall transfusion rates over time was observed, consistent with changes in practice globally. All tumors were reclassified using AJCC's 8th edition while other studies predominantly used the 7th edition. This may cause difficulty in eliciting accurate comparisons between studies, but the eighth edition has been shown to be valid and will be employed in future studies.

Conclusion

Perioperative transfusions are associated with higher cancer stage, comorbidities, and post-operative complications but are not an independent predictor of long-term oncologic or quality of life outcomes after gastroesophagectomy for cancer. Perioperative care physicians should not be biased against transfusion, when required, for fear of worsening long-term outcomes in gastroesophageal cancer patients.

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Compliance with Ethical Standards

Ethics approval was obtained from the Research Ethics Board of McGill University Health Centre in Montreal, Canada (file # 2019-5085).

Conflict of Interest The authors declare that they have no conflicts of interest.

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