Retrospective Cohort Study

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Blood transfusion might not be recommended for gastric cancer patients with pretransfusion minimum hemoglobin values higher than 90 g/l: a real-world study covering 20 years of 13 470 patients

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Background: There was no consistent evidence of whether perioperative blood transfusion (PBT) affects the long-term survival of gastric cancer (GC) patients after undergoing gastrectomy. This study aimed to investigate the effects of PBT on the long-term survival of GC patients, as well as to determine the threshold of PBT and provide evidence for future surgical practice.

Methods: We performed this real-world study of GC patients undergoing gastrectomy at China National Cancer Center from January 1, 2000 to December 30, 2019. Overall survival (OS) curves were plotted using the Kaplan–Meier method and compared statistically using the log-rank test. Univariate and multivariate Cox proportional hazard models were used to determine the risk factors for OS.

Results: In total, 13 470 GC patients undergoing gastrectomy from 2000 to 2019 were included, of whom 3465 (34.6%) GC patients received PBT. PBT ratios declined from 29.1% (114/392) in 2000 to 11.2% in 2019 (149/1178), with the highest blood transfusion ratio in 2005 at 43.7% (220/504). For patients transfused with red blood cells, the median value of hemoglobin (Hb) before transfusion in the PBT group decreased from 110 g/l in 2000 to 87 g/l in 2019. Compared with patients who not receiving PBT, PBT group are more likely to be older ($\geq$65, 39.1% vs. 30.1%, $P<0.001$), open operation (89.7% vs. 78.1%, $P<0.001$), higher American Society of Anesthesiologists score (>2, 25.3% vs. 14.9%, $P<0.001$) and in the later pTNM stage (pTNM stage III, 68.5% vs. 51.5%, $P<0.001$). Results of multivariable Cox regression analysis showed that PBT was an independent prognostic factor for worse OS in GC patients undergoing gastrectomy [HR = 1.106, 95% confidence interval (CI): 1.01–1.211, $P=0.03$). After stratified according to tumor stage, we found that PBT group had a worse prognosis only in pTNM stage III (HR = 1.197, 95% CI: 1.119–1.281, $P<0.001$). OS was obviously poor in the PBT group when Hb levels were higher than 90 g/l (90 g/l < Hb $\leq$ 120 g/l: HR = 1.196, 95% CI: 1.090–1.313, $P<0.001$; Hb > 120 g/l: HR = 1.207, 95% CI: 1.098–1.327, $P<0.001$), while there was no difference between the two groups when Hb levels were lower than or equal to 90 g/l (Hb $\leq$ 90 g/l: HR = 1.162, 95% CI: 0.985–1.370, $P=0.075$).

Conclusion: In conclusion, PBT was an independent prognostic factor for worse OS. Blood transfusion might not be recommended for GC patients with perioperative minimum Hb values higher than 90 g/l.

Keywords: gastric cancer, long-term survival, perioperative blood transfusion, transfusion trend, transfusion trigger

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2024) 110:7020–7033

Received 24 January 2024; Accepted 15 April 2024

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 17 May 2024

http://dx.doi.org/10.1097/JS9.0000000000001535

Introduction

PBT represented the most common treatment for perioperative anemia or blood loss in patients with cancer[1,2]. Patients with GC often suffer from chronic blood loss, acute digestive bleeding, and iron absorption disorder[3,4]. In addition, radical surgery with lymph node dissection might further result in intraoperative blood loss[5]. Thus, PBT was sometimes inevitable for GC patients undergoing gastrectomy[6,7].

The effect of PBT on the long-term prognosis of GC patients undergoing gastrectomy remains controversial. Most studies have shown that PBT had an adverse impact on the long-term survival of GC patients undergoing gastrectomy[8–14], though other studies suggested that PBT was not associated with the long-term survival of GC patients[6,15,16]. Unfortunately, previous studies were limited by the small sample size, ranging from 22[12] to 2884[13].

With increasing evidence of the detrimental effects of PBT on the prognosis of GC patients[8–14], as well as the limited blood resources[17], some experts proposed that a restrictive transfusion strategy and the implementation of patient blood management (PBM) programs[18,19] to minimize the use of transfusion should be implemented as best practice[20–23]. On the other hand, transfusion represented the most common treatment for saving lives who suffered cancer, anemia, or blood loss[24]. Thus, there should be a trade-off for PBT treatment between saving the lives of patients and decreasing the negative impact on prognosis[25]. The American Association of Blood Banks advised using a Hb level of 70 g/l as a transfusion threshold for patients with oncologic disorders[26]. However, the recommendation of 70 g/l was based on the results of different neoplastic or nonneoplastic clinical trials rather than targeted for GC patients. Others recommend no need for transfusion in GC patients when the Hb level is > 100 g/l because of the higher risk of postoperative complications and poor survival outcomes in GC patients[27]. In this context, Hb as a trigger for transfusion is left in a gray area between 70 and 100 g/l, for which no practice recommendation is given.

As such, we conducted this real-world study covering 20 years, including 13 470 GC patients in China National Cancer Center, with the primary aim of evaluating the effect of PBT on long-term survival of GC patients undergoing gastrectomy and also exploring the trigger of Hb for transfusion in GC patients to provide evidence for PBT strategies in surgical practice.

HIGHLIGHTS

- Perioperative blood transfusion (PBT) affects the long-term prognosis of gastric cancer (GC) patients.
- PBT affects the long-term prognosis of stage III GC patients especially.
- PBT might not be recommended for GC patients with hemoglobin (Hb) values > 90 g/l.
- Multicomponent PBT might be more detrimental to long-term survival.

Methods

Study population

All GC patients who underwent radical gastrectomy with a pathological diagnosed gastric adenocarcinoma at China National Cancer Center from January 1, 2000 to December 30, 2019 were retrospectively included. The exclusion criteria were as follows: patients <18 years old, pathologically diagnosed other types of malignancies in the stomach, patients did not receive gastrectomy, patients who received palliative surgery or had distant metastases (M1), (5) patients missed essential clinical data or unknown PBT status and patients with Siewerts I gastro-esophageal junction cancer.

All surgical procedures were performed according to the Japanese guidelines for GC treatment[28], including standardized D2 lymph node dissection.

Definition of PBT

PBT was defined as receiving a transfusion of any components from the admission time to the day of discharge during hospitalization (usually 3–5 days before the operation and 10–14 days after that).

The decision of PBT was made at the discretion of the healthcare team in relation to the clinical conditions of patients. PBT was usually performed based on moderate or severe anemia, inappropriate oxygenation, acute blood loss, or hemodynamic instability.

Data collection and outcomes

Data on clinicopathological characteristics of GC patients were collected retrospectively, including age, sex, BMI, Hb, surgical type and approach, differentiated grade, Lauren or Borrmann type, neurovascular infiltration, grade of American Society of Anesthesiologists physical status classification system, TNM stage, margin, perioperative therapy, and postoperative complications. We further divided all patients into four groups according to time: 2000–2005, 2006–2010, 2011–2015, and 2016–2019, and showed the differences in clinicopathological characteristics of patients within each time period.

The pathological stage was graded in accordance with the seventh American Joint Committee on Cancer (AJCC) TNM Staging System of Gastric Cancer[29]. For patients who are not receiving perioperative blood transfusion (NPBT group), the lowest perioperative Hb values were extracted. For the patients in the PBT group, we recorded the Hb values of the patients before transfusion. For those patients who were transfused more than one time, the Hb values before the first PBT were taken into consideration for evaluation. Besides, to further investigate the effects of different components on prognosis, we further divided the PBT patients into three groups: those who received red blood cell (RBC) only, those who received RBC and other blood components (RBC +), and those who did not receive RBC (no RBC).

The primary outcome was the overall survival (OS) of GC patients. OS was defined by the time from surgery to death from any cause or the last follow-up. Postoperative follow-up was conducted at 3 months after surgery and then annually for 5 years. The last follow-up of the study was in August 2022.

Statistical analyses

Categorical variables were compared using the χ^2 test, and continuous variables were analyzed by Student's t test. OS curves were plotted using the Kaplan–Meier method and compared using of the log-rank test. Univariate and multivariate Cox proportional hazard models were used to determine the risk factors affecting

Table 1

Characteristics of patients undergoing gastrectomy between perioperative blood transfusion and not receiving perioperative blood transfusion groups from the China National Cancer Center from 2000 to 2019.

	Total		
Procedure year	**PBT ($n=3465$)**	**NPBT ($n=10\,005$)**	***P***
Individuals			
Sex			0.012
Male	2509 (72.4%)	7461 (74.6%)	
Female	956 (27.6%)	2544 (25.4%)	
Age			< 0.001
18–40	205 (5.9%)	712 (7.1%)	
41–64	1903 (54.9%)	6278 (62.8%)	
≥ 65	1356 (39.1%)	3012 (30.1%)	
Smoking			< 0.001
Yes	1297 (37.8%)	4460 (45.1%)	
No	2130 (62.2%)	5425 (54.9%)	
Drinking			< 0.001
Yes	1065 (31.2%)	3742 (38.0%)	
No	2351 (68.8%)	6111 (62.0%)	
BMI			< 0.001
< 18.5	267 (7.9%)	437 (4.4%)	
18.5–22.9	1352 (39.8%)	3546 (36.0%)	
23–27.4	1371 (40.3%)	4489 (45.6%)	
≥ 27.5	411 (12.1%)	1380 (14.0%)	
Surgical type			< 0.001
Proximal GC	1385 (40.8%)	3729 (38.3%)	
Distal GC	1348 (39.7%)	4841 (49.7%)	
Total GC	519 (15.3%)	1016 (10.4%)	
Gastric stump cancer/others	141 (4.2%)	157 (1.6%)	
Surgical approach			< 0.001
Open	3035 (89.7%)	7585 (78.1%)	
Laparoscopy assisted	255 (7.5%)	1572 (16.2%)	
Conversion	32 (0.9%)	93 (1.0%)	
Total laparoscopy	60 (1.8%)	464 (4.8%)	
Differentiated grade			0.056
Poorly/undifferentiated	1599 (49.6%)	4744 (51.4%)	
Moderately	1483 (46.0%)	4029 (43.7%)	
Well	142 (4.4%)	453 (4.9%)	
Signet cell			< 0.001
Yes	858 (25.6%)	3032 (31.4%)	
No	2497 (74.4%)	6610 (68.6%)	
Vascular invasion			0.004
Yes	1284 (38.8%)	3416 (35.8%)	
No	2050 (61.5%)	6142 (64.3%)	
Nerve invasion			< 0.001
Yes	790 (23.6%)	3188 (33.1%)	
No	2552 (76.4%)	6444 (66.9%)	
ASA grade			< 0.001
1	146 (4.4%)	582 (6.1%)	
2	2342 (70.4%)	7581 (79.0%)	
3	808 (24.3%)	1415 (14.7%)	
4/5	32 (1.0%)	21 (0.2%)	
pT stage			< 0.001
0	6 (0.2%)	50 (0.5%)	
I	364 (10.7%)	2184 (22.3%)	
II	285 (8.4%)	1237 (12.6%)	
III	863 (25.4%)	2427 (24.7%)	
IV	1872 (55.2%)	3913 (39.9%)	
pN stage			< 0.001
0	919 (26.9%)	3777 (38.3%)	
I	563 (16.5%)	1668 (16.9%)	
II	712 (20.9%)	1803 (18.3%)	
III	1217 (35.7%)	2607 (26.4%)	
pTNM stage			< 0.001

Table 1

(*Continued*)

	Total		
Procedure year	**PBT ($n=3465$)**	**NPBT ($n=10\ 005$)**	***P***
0	6 (0.2%)	44 (0.4%)	
I	486 (14.0%)	2689 (26.9%)	
II	527 (15.2%)	1939 (19.4%)	
III	2375 (68.5%)	5152 (51.5%)	
Lauren			< 0.001
Intestinal type	555 (16.0%)	2143 (21.4%)	
Diffuse type	485 (14.0%)	2272 (22.7%)	
Mix type	352 (10.1%)	1568 (15.7%)	
Unknown	2073 (59.9%)	4022 (40.2%)	
Borrmann			< 0.001
I	296 (8.5%)	795 (7.9%)	
II	1099 (31.7%)	3024 (30.2%)	
III	1090 (31.5%)	2842 (28.4%)	
IV	367 (10.6%)	652 (6.5%)	
Unknown	613 (17.7%)	2692 (26.9%)	
Margin			< 0.001
Negative	3254 (95.9%)	9571 (97.8%)	
Positive	138 (4.1%)	220 (2.2%)	
Neoadjuvant therapy			0.021
Yes	230 (6.8%)	782 (8.0%)	
No	3154 (93.2%)	8961 (92.0%)	
Adjuvant therapy			< 0.001
Yes	1241 (36.7%)	3844 (39.5%)	
No	235 (6.9%)	1094 (11.2%)	
Unknown	1906 (56.4%)	4805 (49.3%)	
Complications			< 0.001
Yes	204 (5.9%)	343 (3.4%)	
No	3261 (94.1%)	9662 (96.6%)	
Perioperative therapy			< 0.001
Yes	1311 (85.6%)	4075 (79.4%)	
No	221 (14.4%)	1057 (20.6%)	

	2000–2005			2006–2010		
Procedure year	PBT	NPBT	*P*	PBT	NPBT	*P*
Individuals						
Sex			0.142			0.069
Male	581 (69.7%)	1105 (72.6%)		835 (73.1%)	1466 (76.0%)	
Female	252 (30.3%)	417 (27.4%)		308 (26.9%)	463 (24.0%)	
Age			0.05			< 0.001
18–40	57 (6.8%)	122 (8.0%)		78 (6.8%)	144 (7.5%)	
41–64	440 (52.8%)	862 (56.6%)		599 (52.5%)	1234 (64.1%)	
≥ 65	336 (40.3%)	538 (35.3%)		465 (40.7%)	548 (28.5%)	
Smoking			0.002			0.308
Yes	248 (29.9%)	547 (36.1%)		387 (34.0%)	686 (35.9%)	
No	582 (70.1%)	970 (63.9%)		750 (66.0%)	1227 (64.1%)	
Drinking			0.026			0.544
Yes	195 (23.5%)	420 (27.7%)		284 (25.1%)	497 (26.1%)	
No	636 (76.5%)	1097 (72.3%)		849 (74.9%)	1410 (73.9%)	
BMI			0.008			< 0.001
< 18.5	73 (8.9%)	80 (5.4%)		89 (7.9%)	92 (4.8%)	
18.5–22.9	303 (37.0%)	582 (39.0%)		479 (42.7%)	670 (35.0%)	
23–27.4	355 (43.3%)	646 (43.3%)		415 (37.0%)	877 (45.8%)	
≥ 27.5	88 (10.7%)	184 (12.3%)		139 (12.4%)	274 (14.3%)	
Surgical type			< 0.001			< 0.001
Proximal GC	342 (42.5%)	703 (48.8%)		487 (43.2%)	785 (41.7%)	
Distal GC	308 (38.3%)	619 (43.0%)		429 (38.1%)	917 (48.7%)	
Total GC	102 (12.7%)	78 (5.4%)		174 (15.4%)	153 (8.1%)	
Gastric stump cancer/others	53 (6.6%)	40 (2.8%)		37 (3.3%)	28 (1.5%)	
Surgical approach			0.455			0.32
Open	802 (100.0%)	1435 (99.9%)		1108 (98.5%)	1862 (98.6%)	

Table 1

(*Continued*)

	Total					
Procedure year	**PBT ($n=3465$)**	**NPBT ($n=10\,005$)**	***P***			
Laparoscopy assisted	0 (0.0%)	1 (0.1%)		11 (1.0%)	21 (1.1%)	
Conversion	–	–		2 (0.2%)	0 (0.0%)	
Total laparoscopy	–	–		4 (0.4%)	6 (0.3%)	
Differentiated grade			0.218			0.637
Poorly/undifferentiated	375 (49.8%)	626 (47.5%)		553 (51.1%)	922 (52.2%)	
Moderately	344 (45.7%)	609 (46.2%)		472 (43.6%)	741 (42.0%)	
Well	34 (4.5%)	82 (6.2%)		57 (5.3%)	102 (5.8%)	
Signet cell			0.011			0.002
Yes	166 (20.9%)	364 (25.7%)		269 (24.1%)	549 (29.2%)	
No	630 (79.1%)	1055 (74.3%)		849 (75.9%)	1329 (70.8%)	
Vascular invasion			0.977			< 0.001
Yes	280 (35.3%)	366 (25.8%)		342 (30.6%)	410 (21.8%)	
No	513 (64.7%)	1050 (74.2%)		774 (69.4%)	1468 (78.2%)	
Nerve invasion			< 0.001			0.017
Yes	13 (1.6%)	23 (1.6%)		97 (8.7%)	119 (6.3%)	
No	780 (98.4%)	1394 (98.4%)		1020 (91.3%)	1758 (93.7%)	
ASA grade			< 0.001			< 0.001
1	34 (4.3%)	90 (6.5%)		46 (4.2%)	148 (8.0%)	
2	496 (63.3%)	966 (69.9%)		693 (62.7%)	1280 (68.8%)	
3	239 (30.5%)	316 (22.9%)		356 (32.2%)	428 (23.0%)	
4/5	14 (1.8%)	10 (0.7%)		10 (0.9%)	4 (0.2%)	
pT stage			< 0.001			< 0.001
0	–	–		0 (0.0%)	1 (0.1%)	
I	62 (7.6%)	220 (15.0%)		102 (9.1%)	382 (20.2%)	
II	63 (7.8%)	153 (10.4%)		70 (6.3%)	220 (11.6%)	
III	3 (0.4%)	12 (0.8%)		307 (27.5%)	460 (24.3%)	
IV	683 (84.2%)	1086 (73.8%)		636 (57.0%)	827 (43.8%)	
pN stage			0.002			< 0.001
0	218 (26.7%)	464 (31.2%)		281 (25.0%)	693 (36.5%)	
I	129 (15.8%)	276 (18.6%)		198 (17.6%)	320 (16.9%)	
II	169 (20.7%)	305 (20.5%)		234 (20.9%)	368 (19.4%)	
III	302 (36.9%)	441 (29.7%)		409 (36.5%)	518 (27.3%)	
pTNM stage			< 0.001			< 0.001
0	–	–		–	–	
I	91 (11.2%)	280 (18.9%)		129 (11.6%)	482 (25.5%)	
II	40 (4.9%)	98 (6.6%)		170 (15.2%)	291 (15.4%)	
III	682 (83.9%)	1102 (74.5%)		817 (73.2%)	1118 (59.1%)	
Lauren			0.056			0.186
Intestinal type	2 (0.2%)	0 (0.0%)		24 (2.1%)	64 (3.3%)	
Diffuse type	–	–		39 (3.4%)	66 (3.4%)	
Mix type	–	–		12 (1.0%)	28 (1.5%)	
Unknown	831 (99.8%)	1522 (100.0%)		1068 (93.4%)	1771 (91.8%)	
Borrmann			< 0.001			< 0.001
I	78 (9.4%)	149 (9.8%)		85 (7.4%)	126 (6.5%)	
II	328 (39.4%)	571 (37.5%)		358 (31.3%)	587 (30.4%)	
III	198 (23.8%)	351 (23.1%)		379 (33.2%)	558 (28.9%)	
IV	118 (14.2%)	149 (9.8%)		130 (11.4%)	157 (8.1%)	
Unknown				191 (16.7%)	501 (26.0%)	
Margin			0.005			0.054
Negative	750 (92.0%)	1409 (94.9%)		1078 (96.9%)	1841 (98.0%)	
Positive	65 (8.0%)	75 (5.1%)		35 (3.1%)	38 (2.0%)	
Neoadjuvant therapy			< 0.001			0.903
Yes	12 (1.5%)	3 (0.2%)		19 (1.7%)	33 (1.7%)	
No	790 (98.5%)	1431 (99.8%)		1107 (98.3%)	1856 (98.3%)	
Adjuvant therapy			0.038			< 0.001
Yes	265 (33.0%)	488 (34.0%)		353 (31.4%)	691 (36.6%)	
No	51 (6.4%)	132 (9.2%)		46 (4.1%)	118 (6.2%)	
Unknown	487 (60.6%)	816 (56.8%)		725 (64.5%)	1080 (57.2%)	
Complications			< 0.001			< 0.001
Yes	32 (3.8%)	18 (1.2%)		61 (5.3%)	22 (1.1%)	

Table 1

(*Continued*)

	Total					
Procedure year	**PBT ($n=3465$)**	**NPBT ($n=10\,005$)**	***P***			
No	801 (96.2%)	1504 (98.8%)		1082 (94.7%)	1907 (98.9%)	
Perioperative therapy			0.019			0.127
Yes	271 (85.2%)	490 (78.9%)		360 (88.9%)	704 (85.7%)	
No	47 (14.8%)	131 (21.1%)		45 (11.1%)	117 (14.3%)	
		2011–2015			2016–2019	
Individuals						
Sex			0.196			0.777
Male	747 (73.7%)	2671 (75.7%)		346 (72.7%)	2219 (73.3%)	
Female	266 (26.3%)	856 (24.3%)		130 (27.3%)	808 (26.7%)	
Age			< 0.001			0.543
18–40	46 (4.5%)	255 (7.2%)		24 (5.0%)	191 (6.3%)	
41–64	561 (55.4%)	2299 (65.2%)		303 (63.7%)	1883 (62.2%)	
≥ 65	406 (40.1%)	973 (27.6%)		149 (31.3%)	953 (31.5%)	
Smoking			< 0.001			0.319
Yes	417 (41.9%)	1735 (49.8%)		245 (52.7%)	1492 (50.2%)	
No	578 (58.1%)	1748 (50.2%)		220 (47.3%)	1480 (49.8%)	
Drinking			0.001			0.422
Yes	367 (37.2%)	1485 (42.9%)		219 (47.1%)	1340 (45.1%)	
No	620 (62.8%)	1973 (57.1%)		246 (52.9%)	1631 (54.9%)	
BMI			< 0.001			0.435
< 18.5	84 (8.4%)	131 (3.7%)		21 (4.5%)	134 (4.5%)	
18.5–22.9	387 (38.8%)	1237 (35.4%)		183 (39.6%)	1057 (35.8%)	
23–27.4	398 (39.9%)	1604 (45.9%)		203 (43.9%)	1362 (46.2%)	
≥ 27.5	129 (12.9%)	525 (15.0%)		55 (11.9%)	397 (13.5%)	
Surgical type			< 0.001			0.259
Proximal GC	429 (43.1%)	1394 (40.1%)		127 (27.3%)	847 (28.8%)	
Distal GC	364 (36.5%)	1698 (48.8%)		247 (53.1%)	1607 (54.6%)	
Total GC	158 (15.9%)	347 (10.0%)		85 (18.3%)	438 (14.9%)	
Gastric stump cancer/others	45 (4.5%)	37 (1.1%)		6 (1.3%)	52 (1.8%)	
Surgical approach			< 0.001			0.007
Open	855 (86.0%)	2755 (79.5%)		270 (58.6%)	1533 (52.4%)	
Laparoscopy assisted	112 (11.3%)	596 (17.2%)		132 (28.6%)	954 (32.6%)	
Conversion	14 (1.4%)	32 (0.9%)		16 (3.5%)	61 (2.1%)	
Total laparoscopy	13 (1.3%)	82 (2.4%)		43 (9.3%)	376 (12.9%)	
Differentiated grade			0.005			0.639
Poorly/undifferentiated	439 (46.7%)	1661 (50.5%)		232 (51.8%)	1535 (53.8%)	
Moderately	461 (49.0%)	1433 (43.5%)		206 (46.0%)	1246 (43.7%)	
Well	41 (4.4%)	197 (6.0%)		10 (2.2%)	72 (2.5%)	
Signet cell			0.001			0.801
Yes	272 (27.7%)	1150 (33.3%)		151 (32.9%)	969 (33.5%)	
No	710 (72.3%)	2302 (66.7%)		308 (67.1%)	1924 (66.5%)	
Vascular invasion			0.001			0.01
Yes	409 (41.9%)	1237 (35.9%)		253 (56.3%)	1403 (49.8%)	
No	567 (58.1%)	2211 (64.1%)		196 (43.7%)	1413 (50.2%)	
Nerve invasion			0.107			0.769
Yes	408 (41.8%)	1342 (38.9%)		272 (59.6%)	1704 (58.9%)	
No	568 (58.2%)	2104 (61.1%)		184 (40.4%)	1188 (41.1%)	
ASA grade			< 0.001			0.231
1	46 (4.7%)	261 (7.6%)		20 (4.4%)	83 (2.9%)	
2	758 (77.0%)	2736 (79.4%)		395 (86.8%)	2599 (89.3%)	
3	173 (17.6%)	444 (12.9%)		40 (8.8%)	227 (7.8%)	
4/5	8 (0.8%)	4 (0.1%)		0 (0.0%)	3 (0.1%)	
pT stage			< 0.001			0.02
0	1 (0.1%)	11 (0.3%)		5 (1.1%)	38 (1.3%)	
I	110 (11.0%)	884 (25.4%)		90 (19.3%)	698 (23.6%)	
II	99 (9.9%)	461 (13.2%)		53 (11.4%)	403 (13.6%)	
III	445 (44.6%)	1231 (35.3%)		108 (23.2%)	724 (24.4%)	
IV	343 (34.4%)	900 (25.8%)		210 (45.1%)	1100 (37.1%)	
pN stage			< 0.001			0.017
0	267 (26.6%)	1425 (40.8%)		153 (32.6%)	1195 (40.2%)	

Table 1

(*Continued*)

	Total					
Procedure year	**PBT ($n=3465$)**	**NPBT ($n=10\,005$)**	***P***			
I	154 (15.4%)	576 (16.5%)		82 (17.5%)	496 (16.7%)	
II	215 (21.5%)	608 (17.4%)		94 (20.0%)	522 (17.5%)	
III	366 (36.5%)	886 (25.4%)		140 (29.9%)	762 (25.6%)	
pTNM stage			< 0.001			0.008
0	1 (0.1%)	9 (0.3%)		5 (1.1%)	35 (1.2%)	
I	157 (15.7%)	1077 (31.0%)		109 (23.4%)	850 (28.7%)	
II	218 (21.8%)	828 (23.8%)		99 (21.2%)	722 (24.4%)	
III	623 (62.4%)	1574 (45.2%)		253 (54.3%)	1358 (45.8%)	
Lauren			0.057			0.2
Intestinal type	375 (37.0%)	1151 (32.6%)		156 (32.8%)	928 (30.7%)	
Diffuse type	303 (29.9%)	1173 (33.3%)		141 (29.6%)	1033 (34.1%)	
Mix type	224 (22.1%)	812 (23.0%)		116 (24.4%)	728 (24.1%)	
Unknown	111 (11.0%)	391 (11.1%)		63 (13.2%)	338 (11.2%)	
Borrmann			< 0.001			0.529
I	96 (9.5%)	242 (6.9%)		37 (7.8%)	278 (9.2%)	
II	282 (27.8%)	1011 (28.7%)		131 (27.5%)	855 (28.2%)	
III	357 (35.2%)	1051 (29.8%)		156 (32.8%)	882 (29.1%)	
IV	95 (9.4%)	177 (5.0%)		24 (5.0%)	169 (5.6%)	
Unknown	183 (18.1%)	1046 (29.7%)		128 (26.9%)	843 (27.8%)	
Margin			0.004			0.474
Negative	964 (96.7%)	3421 (98.2%)		462 (98.9%)	2900 (98.5%)	
Positive	33 (3.3%)	63 (1.8%)		5 (1.1%)	44 (1.5%)	
Neoadjuvant therapy			< 0.001			0.285
Yes	117 (11.8%)	285 (8.2%)		82 (17.6%)	461 (15.6%)	
No	872 (88.2%)	3182 (91.8%)		385 (82.4%)	2492 (84.4%)	
Adjuvant therapy			< 0.001			0.134
Yes	410 (41.5%)	1398 (40.4%)		213 (45.7%)	1267 (42.8%)	
No	103 (10.4%)	538 (15.5%)		35 (7.5%)	306 (10.3%)	
Unknown	476 (48.1%)	1525 (44.1%)		218 (46.8%)	1384 (46.8%)	
Complications			< 0.001			0.018
Yes	69 (6.8%)	122 (3.5%)		42 (8.8%)	181 (6.0%)	
No	944 (93.2%)	3405 (96.5%)		434 (91.2%)	2846 (94.0%)	
Perioperative therapy			< 0.001			0.072
Yes	446 (82.3%)	1481 (73.7%)		234 (87.6%)	1400 (83.3%)	
No	96 (17.7%)	528 (26.3%)		33 (12.4%)	281 (16.7%)	

ASA, American Society of Anesthesiologists; GC, gastric cancer; NPBT, not receiving perioperative blood transfusion; PBT, perioperative blood transfusion; pT stage: pathological T stage; pN stage: pathological N stage; pTNM, pathological TNM stage.

the OS. Factors with a P value <0.1 in the univariate Cox analysis will be included in the multivariate Cox analysis. P value <0.05 in the multivariate analysis was considered significant.

R software, version 4.3.0 and GraphPad Prism, version 9.4.1, were used for all statistical analyses.

The work had been reported in line with the STROCSS criteria[30] (Supplemental Digital Content 1, http://links.lww.com/JS9/C588).

Results

Clinicopathological characteristics

The clinicopathological characteristics of the 13 470 patients are listed in Table 1, of whom 3465 (34.6%) GC patients received PBT. Compared with the NPBT group, the PBT group was more likely to be older (≥65, 39.1% vs. 30.1%, $P<0.001$), higher American Society of Anesthesiologists grade (grade >2, 25.3% vs. 14.9%, $P<0.001$) and in the later pTNM stage (pT4, 55.2% vs. 39.9%, $P<0.001$; pN3, 35.7% vs. 26.4%, $P<0.001$; pTNM stage III, 68.5% vs. 51.5%, $P<0.001$). Relatively higher percentages of open surgery (89.7% vs. 78.1%, $P<0.001$), positive surgical margin (4.1% vs. 2.2%, $P<0.001$), Borrmann IV (10.6% vs. 6.5%, $P<0.001$), and perioperative therapy (85.6% vs. 79.4%, $P<0.001$) were shown in patients with PBT. Moreover, the incidence of postoperative complications was higher in the PBT group (5.9% vs. 3.4%, $P<0.001$).

Time trends of PBT ratios for GC patients

PBT ratios declined from 29.1% (114/392) in 2000 to 11.2% in 2019 (149/1178), with the highest blood transfusion rate in 2005 at 43.7% (220/504). The transfusion ratios of GC patients have been less than 20% since 2014 (17.9%) (Fig. 1A).

The amount of transfusions of various blood components also decreased over 20 years (Table S1, Supplemental Digital Content 2, http://links.lww.com/JS9/C589). The mean volumes of RBC transfusion declined from 5.37 U (1–44 U) in 2000–2005 to 3.41 U (1–20 U) in 2016–2019. The mean volumes of fresh frozen

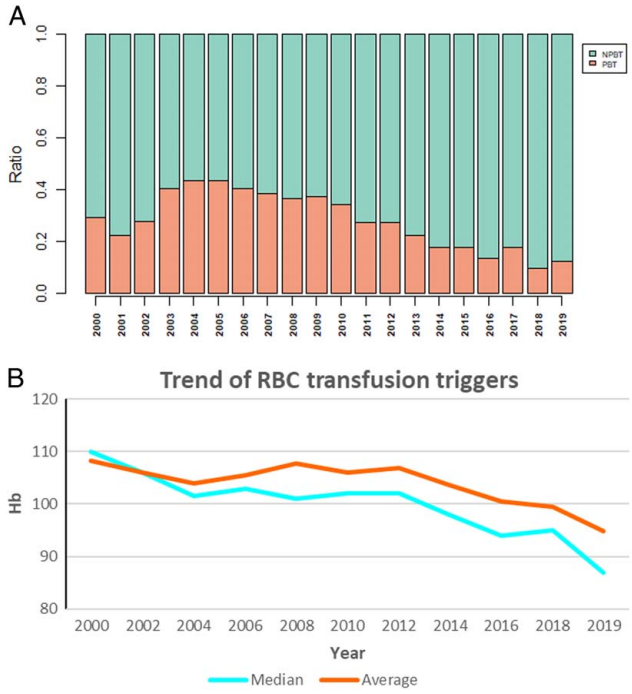

Figure 1. (A) The PBT ratios of GC patients undergoing gastrectomy from 2000 to 2019. (B) The RBC transfusion triggers of GC patients undergoing gastrectomy from 2000 to 2019. GC, gastric cancer; PBT, perioperative blood transfusion; RBC, red blood cell.

plasma transfusion declined from 1208.4 ml (100–13 600 ml) in 2000–2005 to 548.52 ml (100–4800 ml) in 2016–2019.

For patients transfused with RBC in the PBT group, the changes in median Hb values and the average Hb values before transfusion are shown in Figure 1B. We found that the median Hb values decreased from 110 g/l in 2000 to 87 g/l in 2019, and the average Hb values decreased from 108 to 94 g/l.

Long-term survival of GC patients with PBT group and NPBT group

Figure 2 shows the Kaplan–Meier curves for OS. The median OS for the entire cohort was 60 months. The 1-year, 3-year, 5-year, and 10-year OS rates in the PBT group were 88.1%, 62.2%, 51.9%, and 36.5%, respectively, and were less than those in the NPBT group, which were 93.2%, 74.1%, 64.8%, and 49.9%, respectively ($P < 0.001$) (Fig. 2A).

Univariable and multivariable Cox proportional hazards models were used to determine the prognostic factors for OS in the entire cohort (Table 2). Variables with a P value less than 0.1 in the univariable analysis were involved in the multivariable analysis. In the multivariable analysis, the independent predictor for poor OS included PBT (HR = 1.106, 95% CI: 1.01–1.211, $P = 0.03$), age ≥ 65 (HR = 1.307, 95% CI: 1.104–1.546, $P = 0.002$), smoking (HR = 1.15, 95% CI: 1.038–1.275, $P = 0.008$), surgical type (total gastrectomy: HR = 1.263, 95% CI: 1.12–1.424, $P < 0.001$), Signet cell (HR = 1.224, 95% CI: 1.116–1.343, $P < 0.001$), nerve invasion (HR = 1.24, 95% CI: 1.128–1.362, $P < 0.001$), later pN stage (N3: HR = 3.07, 95% CI: 2.671–3.528, $P < 0.001$), and positive margin (HR = 1.239, 95% CI: 1.013–1.515, $P < 0.037$). Additional factors associated with better OS in GC patients included female (HR = 0.877, 95% CI: 0.787–0.977, $P = 0.017$), BMI > 27.5(HR = 0.656, 95% CI: 0.534–0.806, $P < 0.001$), well differentiation (HR = 0.758, 95% CI: 0.585–0.982, $P < 0.036$), earlier pT stage (T3 vs. T4: HR = 0.838, 95% CI: 0.765–0.919, $P < 0.001$).

Considering that repeated surgery would intuitively result in more blood loss, we excluded patients with gastric stump cancer and performed further analyses. In the cohort of 13 239 patients, we found that PBT was still the independent predictor for poor OS (HR = 1.103, 95% CI: 1.006–1.211, $P = 0.038$) (Supplementary Table 2–3, Supplemental Digital Content 3, http://links.lww.com/JS9/C590, Supplemental Digital Content 4, http://links.lww.com/JS9/C591). Besides, the types of neoadjuvant therapy regimes during the 2000–2019 time period had been changed. We included GC patients with neoadjuvant therapy and we found that PBT was associated with poor OS (HR = 1.381, 95% CI: 1.104–1.728, $P = 0.005$) (Supplementary Table 4–5, Supplemental Digital Content 5, http://links.lww.com/JS9/C592, Supplemental Digital Content 6, http://links.lww.com/JS9/C593).

Long-term survival between the PBT group and the NPBT group stratified by pTNM stage

After stratifying by pTNM stage, the Kaplan–Meier curve showed that OS was worse in the PBT group than in the NPBT group in both stages I, II, and III (stage I: $P < 0.001$; stage II: $P = 0.048$; stage III: $P < 0.001$) (Fig. 2B–D). In the multivariable analysis after stratifying in stage III GC patients, PBT was an independent predictor for worse OS (stage III, HR = 1.197, 95% CI: 1.119–1.281, $P < 0.001$), while PBT was not associated with OS when GC patients were in stages I and II (stage I, HR = 1.11, 95% CI: 0.864–1.425, $P = 0.414$; stage II, HR = 1.023, 95% CI: 0.86–1.218, $P = 0.794$) (Table 3).

Long-term survival between the PBT group and the NPBT group stratified by different perioperative minimum Hb level

To further compared OS for GC patients with or without PBT at different Hb concentration thresholds, we conducted stratified comparisons according to Hb values ≤ 90, 90–120, and > 120 g/l (Fig. 3). Kaplan–Meier curve showed that PBT group GC patients had worse OS, regardless of the Hb levels (Hb ≤ 90 g/l: $P < 0.001$; 90 g/l <Hb ≤ 120 g/l: $P < 0.001$; Hb > 120 g/l: $P < 0.001$). In the multivariable Cox analysis after stratifying by different Hb level, we found that PBT was an independent predictor for worse OS when perioperative minimum Hb levels higher than 90 g/l (Hb > 90 g/l and Hb ≤ 120 g/l: HR = 1.196, 95% CI: 1.090–1.313, $P < 0.001$; Hb > 120 g/l: HR = 1.207, 95% CI: 1.098–1.327, $P < 0.001$). When Hb levels less than or equal to 90 g/l, PBT was not associated with OS (Hb ≤ 90 g/l: HR = 1.162, 95% CI: 0.985–1.370, $P = 0.075$) (Table 4).

Long-term survival in the PBT group stratified by different PBT components

Figure 4 shows the Kaplan–Meier curves of OS in the PBT group receiving different blood components. Compared to the patients only receiving RBC, patients receiving RBC + had a worse OS (HR = 1.293, 95% CI: 1.159–1.442, $P < 0.001$), while there was no difference between patients who received only RBCs and those who received no RBC (HR = 1.033, 95% CI: 0.877–1.217, $P = 0.695$) (Table 5).

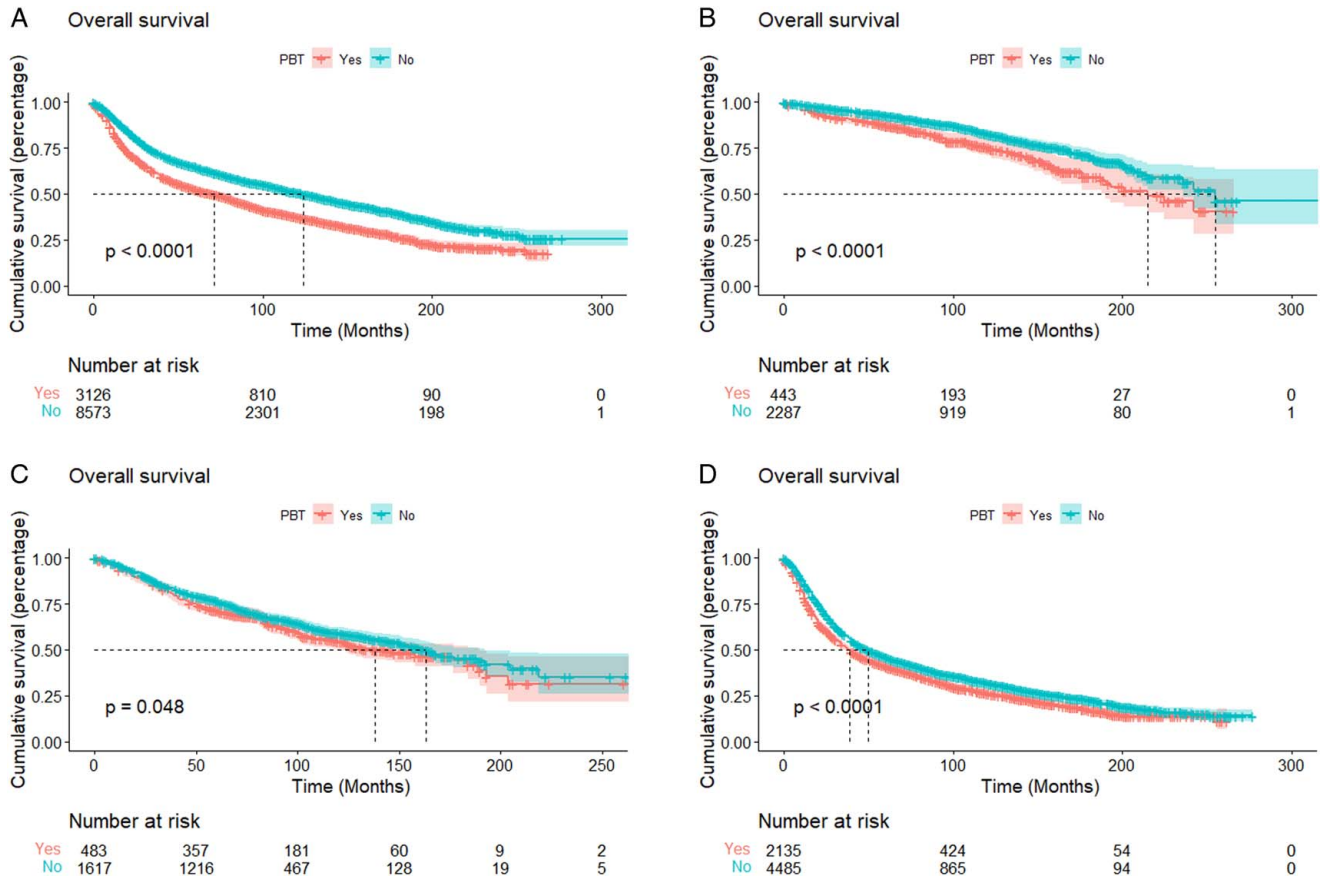

Figure 2. (A) The Kaplan–Meier curves of overall survival of the entire cohort between the PBT group and the NPBT group. (B) The Kaplan–Meier curves of overall survival of stage I between the PBT group and the NPBT group. (C) The Kaplan–Meier curves of overall survival of stage II between the PBT group and the NPBT group. (D) The Kaplan–Meier curves of overall survival of stage III between the PBT group and the NPBT group. NPBT, not receiving perioperative blood transfusion; PBT, perioperative blood transfusion.

Discussion

This real-world study systematically investigated the effects of PBT on long-term survival in GC patients and identified the Hb trigger before considering PBT. To the best of our knowledge, our analysis represented the largest evaluation of PBT in terms of survival outcomes in GC patients. A primary finding was that compared to the NPBT group, PBT group had a worse OS, especially in stage III GC patients. Moreover, PBT might not be recommended for GC patients with pretransfusion minimum Hb values higher than 90 g/l.

Several studies investigating the effect of PBT on the long-term survival of GC patients were published with conflicting results[6,8–16]. To explore the correlation, we conducted a meta-analysis previously and systematically reviewed the related studies from 1989 to 2021, suggesting that PBT was a predictor for worse OS. Our large-scale retrospective cohort study was conducted further and showed similar results to the meta-analysis. The mechanisms by which PBT impacted the prognosis of GC patients were still unclear. It was an accepted fact that blood products caused profound negative effects on the human immune system, a condition termed transfusion-related immune modulation[31,32]. Potential causes of transfusion-induced immune dysfunction include suppression of cytotoxic cell and monocyte activity, inhibition of interleukin-2 production, and increased suppressor T-cell activity and immunosuppressive prostaglandins[33–36]. A prospective study showed that serum neopterin, interferon-γ, percentages of T-cell subsets (CD3+, CD4+), and CD4+/CD8+ ratio decreased in GC patients receiving gastrectomy[37]. Transfusion-related immune modulation might underlie the progression of minimal residual disease and metastasis[31,38]. In addition, blood transfusion could promote increases in interleukin-6[39], vascular endothelial growth factor[40], hepatocyte growth factor[41], and the proliferation of tumor cells through inducing angiogenesis[16,42]. What's more, we found that GC patients who received multicomponent PBT (RBC+) had worse OS. Some researchers have postulated that leukocytes in whole blood or multiple growth factors may contribute to the adverse effects of PBT[43]. The bona fide mechanism of the deleterious prognostic effect of PBT remains elusive.

Patients with gastric stump cancer undergo repeated surgery that may lead to more blood loss and PBT. We excluded patients with gastric stump cancer from the entire cohort and performed further subgroup analyses. The results showed that PBT was still associated with poor prognosis. What is more, to avoid the influence of long time span and different neoadjuvant regimens

Table 2

Univariate and multivariate analysis of factors associated with overall survival following radical gastrectomy.

	Univariate				Multivariate			
Character	**HR**	**Upper**	**Lower**	***P* value**	**HR**	**Upper**	**Lower**	***P***
Individuals								
Sex								
Male	Reference				Reference			
Female	0.882	0.83	0.937	< 0.001	0.877	0.787	0.977	0.017
Age								
18–40	Reference				Reference			
41–64	0.984	0.88	1.101	0.778	0.932	0.797	1.091	0.38
≥ 65	1.539	1.374	1.725	< 0.001	1.307	1.104	1.546	0.002
Smoking								
No	Reference				Reference			
Yes	1.115	1.058	1.175	< 0.001	1.15	1.038	1.275	0.008
Drinking								
No	Reference				Reference			
Yes	1.03	1.003	1.059	0.032	1	0.902	1.107	0.994
BMI								
< 18.5	Reference				Reference			
18.5–22.9	0.83	0.743	0.928	0.001	0.781	0.649	0.939	0.009
23–27.4	0.705	0.631	0.787	< 0.001	0.699	0.581	0.841	< 0.001
≥ 27.5	0.658	0.58	0.747	< 0.001	0.656	0.534	0.806	< 0.001
Surgical type								
Proximal GC	Reference				Reference			
Distal GC	0.558	0.526	0.592	< 0.001	0.714	0.648	0.787	< 0.001
Total GC	1.545	1.43	1.668	< 0.001	1.263	1.12	1.424	< 0.001
Gastric stump cancer	1.119	0.954	1.312	0.167	1.385	1.064	1.801	0.015
Surgical approach								
Open	Reference				Reference			
Laparoscopy assisted	0.617	0.558	0.684	< 0.001	0.938	0.81	1.085	0.388
Conversion	1.207	0.906	1.609	0.199	1.443	1.022	2.037	0.037
Total laparoscopy	0.736	0.597	0.906	0.004	1.204	0.922	1.572	0.172
Differentiated grade								
Poorly/undifferentiated	Reference				Reference			
Moderately	0.795	0.753	0.84	< 0.001	0.937	0.855	1.026	0.16
Well	0.433	0.37	0.507	< 0.001	0.758	0.585	0.982	0.036
Signet cell								
No	Reference				Reference			
Yes	1.105	1.043	1.17	0.001	1.224	1.116	1.343	< 0.001
Vascular invasion								
No	Reference				Reference			
Yes	2.033	1.927	2.146	< 0.001	1.096	1.002	1.199	0.045
Nerve invasion								
No	Reference				Reference			
Yes	1.772	1.672	1.877	< 0.001	1.24	1.128	1.362	< 0.001
ASA grade								
1	Reference				Reference			
2	1.289	1.138	1.461	< 0.001	1.064	0.896	1.263	0.482
3	1.791	1.568	2.047	< 0.001	1.265	1.041	1.537	0.018
4/5	2.09	1.469	2.975	< 0.001	1.354	0.708	2.59	0.359
pT stage*								
IV	Reference				Reference			
0	0.261	0.109	0.628	0.003	0.001	0	3.17E + 24	0.82
I	0.167	0.15	0.187	< 0.001	0.365	0.297	0.448	< 0.001
II	0.286	0.256	0.32	< 0.001	0.502	0.421	0.597	< 0.001
III	0.792	0.746	0.841	< 0.001	0.838	0.765	0.919	< 0.001
pN stage*								
0	Reference				Reference			
I	1.921	1.753	2.105	< 0.001	1.339	1.148	1.562	< 0.001
II	3.081	2.836	3.347	< 0.001	2.069	1.792	2.389	< 0.001
III	5.514	5.123	5.934	< 0.001	3.07	2.671	3.528	< 0.001
Margin								
Negative	Reference				Reference			
Positive	2.329	2.052	2.645	< 0.001	1.239	1.013	1.515	0.037

Table 2

(Continued)

Character	Univariate				Multivariate			
	HR	Upper	Lower	*P* value	HR	Upper	Lower	*P*
Complications								
No	Reference				Reference			
Yes	1.509	1.333	1.707	< 0.001	1.074	0.874	1.321	0.496
Perioperative therapy								
No	Reference				Reference			
Yes	2.112	1.89	2.359	< 0.001	0.945	0.829	1.078	0.402
PBT								
No	Reference				Reference			
Yes	1.477	1.398	1.56	< 0.001	1.106	1.01	1.211	0.03

ASA, American Society of Anesthesiologists; GC, gastric cancer; PBT, perioperative blood transfusion; pTNM, pathological TNM stage.

Table 3

Subgroup analysis of factors associated with overall survival between perioperative blood transfusion and not receiving perioperative blood transfusion groups of different stages.

Prognostic factors	Adjusted		
	HR	95% CI	*P*
pTNM I			
PBT			
No	Reference		
Yes	1.11	0.864–1.425	0.414
pTNM II			
PBT			
No	Reference		
Yes	1.023	0.86–1.218	0.794
pTNM III			
PBT			
No	Reference		
Yes	1.197	1.119–1.281	< 0.001

Adjusted factors: sex, age, smoking, BMI, surgical type, surgical approach, differentiated grade, signet cell, vascular invasion, nerve invasion, American Society of Anesthesiologists grade, TNM stage, margin.

CI, confidence interval; PBT, perioperative blood transfusion.

on the results, we included patients receiving neoadjuvant therapy for further subgroup analysis. The results showed that PBT remained an independent predictor of poor OS. We believe that our conclusions are credible and that effective PBT management is necessary.

Given the mixture of transfusion-related unknowns that may negatively influence cancer patients, a restrictive PBT policy has been advocated for surgical patients with cancer[44]. American Association of Blood Banks International Guidelines suggested a restrictive RBC transfusion strategy in which transfusion was considered when the Hb concentration was less than 70 g/l in those with oncologic disorders[26]. A randomized controlled study of patients admitted to the ICU after major surgery for abdominal cancer published in 2015 suggested that using a Hb threshold of 90 g/l was superior to a restrictive strategy with a Hb threshold of 70 g/l[45]. Unfortunately, the above study did not provide general recommendations for appropriate PBT thresholds targeted for GC patients and did not explore the impact of different PBT thresholds on the long-term survival of patients. In our study, we found that PBT was associated with worse OS when pretransfusion minimum Hb values were higher than 90 g/l. GC patients receiving more restrictive transfusions lower than 90 g/l might be more susceptible to altered oxygen delivery and

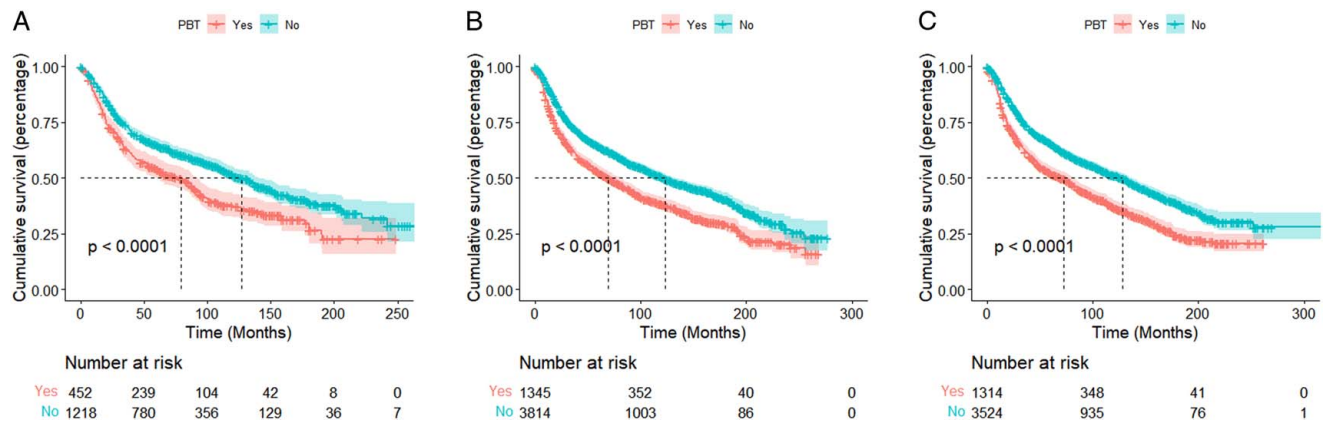

Figure 3. (A) The Kaplan–Meier curves of overall survival between the PBT group and the NPBT group when Hb ≤ 90 g/l. (B) The Kaplan–Meier curves of overall survival between the PBT group and the NPBT group when Hb > 90 g/l and Hb ≤ 120 g/l. (C) The Kaplan–Meier curves of overall survival between the PBT group and the NPBT group when Hb > 120 g/l. Hb, hemoglobin; NPBT, not receiving perioperative blood transfusion; PBT, perioperative blood transfusion.

Table 4

Subgroup analysis of factors associated with overall survival between perioperative blood transfusion and not receiving perioperative blood transfusion groups of perioperative lowest hemoglobin levels (not receiving perioperative blood transfusion group) or lowest pretransfusion hemoglobin levels (perioperative blood transfusion group).

	Adjusted		
Prognostic factors	**HR**	**95% CI**	***P***
Hb ≤ 90g			
PBT			
No	Reference		
Yes	1.162	0.985–1.370	0.075
90 g/l < Hb ≤ 120 g/l			
PBT			
No	Reference		
Yes	1.196	1.090–1.313	< 0.001
Hb > 120 g/l			
PBT			
No	Reference		
Yes	1.207	1.098–1.327	< 0.001

Adjusted factors: sex, age, smoking, BMI, surgical type, surgical approach, differentiated grade, signet cell, vascular invasion, nerve invasion, American Society of Anesthesiologists grade, TNM stage, margin.
CI, confidence interval; Hb, hemoglobin; PBT, perioperative blood transfusion.

impaired tissue oxygenation during the postoperative period, leading to a worse short-term prognosis[45–47]. When the PBT threshold was higher than 90 g/l, immunomodulation and the inflammatory consequences of transfusion might outweigh the possible advantages of improved oxygen delivery and tissue perfusion[48]. Ninety grams per liter might be the inflection point at which transfusions become deleterious and clinical transfusion appropriateness lies in this delicate balance.

In our study, we analyzed the trend of PBT ratios, and we found that there was a significant trend of decreasing ratios of PBT over time, which declined from 29.1% (114/392) in 2000 to 11.2% in 2019 (149/1178), which was consistent with Ecker *et al.*'[5] results, with the highest blood transfusion ratio in 2005 at 43.7% (220/504). The median Hb values before RBC transfusion decreased from 110 g/l in 2000 to 87 g/l in 2019, and the average Hb values before RBC transfusion decreased from 108 to

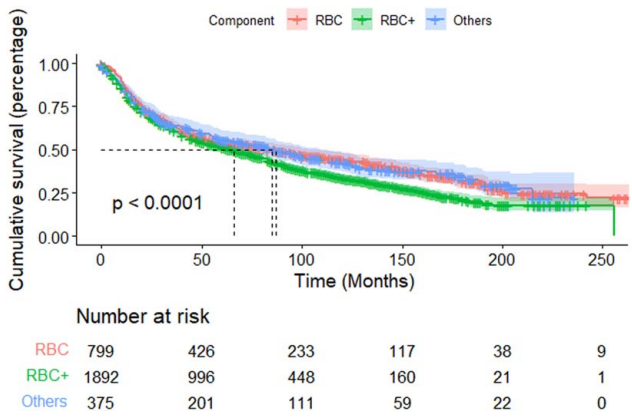

Figure 4. The Kaplan–Meier curves of overall survival receiving different blood components in the PBT group. PBT, perioperative blood transfusion.

Table 5

Multivariate analysis of different perioperative blood transfusion components associated with overall survival in perioperative blood transfusion group.

	Adjusted		
Prognostic factors	**HR**	**95% CI**	***P***
PBT components			
RBC	Reference		
RBC +	1.293	1.159–1.442	< 0.001
Others	1.033	0.877–1.217	0.695

Adjusted factors: sex, age, smoking, BMI, surgical type, surgical approach, differentiated grade, signet cell, vascular invasion, nerve invasion, American Society of Anesthesiologists grade, TNM stage, margin.
CI, confidence interval; PBT, perioperative blood transfusion; RBC, red blood cell.

94 g/l. Changes in trends may represent increasing concern regarding the controversial effects of PBT on GC patients and a commitment to more restrictive transfusion thresholds[49]. Besides, PBM initiatives are increasingly adopted across the globe as part of the standard of treatment[50]. PBM is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety[50]. PBM consists of three pillars: the optimization of RBC mass, including treatments such as erythropoiesis-stimulating agents and iron and vitamin supplements; reduction of blood loss and bleeding by optimizing surgical and anesthetic techniques; and optimization of the patient's physiological tolerance toward anemia by promoting maximum pulmonary and cardiac function[19,51]. The use of PBM might be another important reason for the decline in PBT ratios in recent years.

Our hospital-based study was the largest one to evaluate the effect of PBT on long-term survival outcomes for GC patients to date. What is more, we suggested that a Hb value of 90 g/l might be the trigger point for PBT in GC patients. Several limitations need to be considered in this study. First, the results of this study were limited by the retrospective nature of the study design. Second, the decision for PBT was at the discretion of the surgeon and the anesthesiologist and, therefore, subjective. However, these decisions reflected the standard of care at many tertiary care centers. Besides, we could not specify whether the patient had another blood transfusion before admission or after discharge. This might potentially have had an impact on the patient's long-term survival. However, it was undeniable that as the largest retrospective study to date investigating PBT and long-term prognosis in GC patients, its conclusions were instructive in guiding clinical blood transfusion practice. Our database did not include information on disease-free survival. Further, multicenter, large-scale prospective trials are needed.

Conclusion

In conclusion, PBT was an independent prognostic factor for worse OS. Blood transfusion might not be recommended for GC patients with perioperative minimum Hb values higher than 90 g/l.

Ethical approval

This study was approved by the ethics committee of the National Cancer Center/National Clinical Research Center for Cancer/

Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 17-156/1412).

Consent

Written informed consent was obtained from the patient for publication of this manuscript and accompanying images.

Sources of funding

This work was supported by the National Key R&D Program of China (No. 2017YFC0908300), the 2023 Scientific Research-Project of Chronic Diseases Control and Health Education (No. BJMB0012023024005) and Beijing Nova Program (No. 20220484200).

Author contribution

Y.C., L.Z., and D.Z.: conception/design. W.W., C.S., X.Z., and P.N.: provision of study material or patients. W.W., C.S., and X. H.: collection and/or assembly of data. W.W., X.L., X.Z., and P. N.: data analysis and interpretation. All the authors provide the final approval of the manuscript.

Conflicts of interest disclosure

The authors indicated no financial relationships.

Research registration unique identifying number (UIN)

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The registration was in process:

1. Name of the registry: Chinese Clinical Trial Registry.
2. Unique identifying number or registration ID: ChiCTR 2400089294.
3. Hyperlink to your specific registration (must be publiclyaccessible and will be checked): https://www.chictr.org.cn/bin/project/edit?pid=232620.

Guarantor

Yingtai Chen.

Data availability statement

The data used to support the findings of this study is included within the article in tables.

Provenance and peer review

Not applicable.

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