

Effect of perioperative blood transfusion on complications and prognosis after radical gastrectomy in elderly patients: a retrospective study of 1,666 cases

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Background: Multiple studies have examined the effect of perioperative blood transfusion (BTF) on postoperative complications and the prognosis of gastric cancer patients, but the conclusions remain controversial, and few studies related to elderly patients are present. This study sought to examine the effect of perioperative BTF on postoperative complications and the prognosis of elderly patients who underwent radical gastrectomy.

Methods: The clinical data of 1,666 elderly patients (aged \geq 60 years) at Xijing Hospital from October 2013 to October 2021 were retrospectively analyzed. The patients were stratified into the perioperative BTF group and the perioperative non-BTF group. The clinicopathological characteristics, postoperative complications, and long-term prognoses of the patients were compared.

Results: There were significant differences in terms of sex, tumor location, tumor size, gastrectomy range, tumor differentiation, T stage, N stage, tumor-node-metastasis (TNM) stage, preoperative anemia, and intraoperative blood loss between the two groups (P<0.05). The incidence of postoperative fever in the BTF group was significantly higher than that in the non-BTF group (31.6% *vs.* 15.4%, P<0.001), but there were no significant differences in the other complications between the two groups (P>0.05). The survival analysis showed that in stage III patients, the prognosis of the BTF group was inferior to that of the non-BTF group [the 3-year overall survival (OS) rates of the groups were 33.7% *vs.* 47.9% respectively, P<0.001], while there was no significant difference between the two groups among the stage I and stage II patients (P>0.05). The multivariate analysis indicated that perioperative BTF was not an independent risk factor for prognosis in elderly patients with gastric cancer overall or elderly patients with gastric cancer in stage III (P>0.05).

Conclusions: Perioperative BTF may elevate the incidence of fever but has no significant effect on other complications in elderly patients after radical gastrectomy. Perioperative BTF is not an independent risk factor affecting the postoperative prognosis of elderly patients with gastric cancer.

Keywords: Perioperative blood transfusion (perioperative BTF); gastrectomy; complications; prognosis; elderly

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Liu et al. BTF in elderly patients who underwent radical gastrectomy

Introduction

Gastric cancer is a prevalent form of malignancy affecting the digestive tract. Currently, surgery stands as the sole possible cure for resectable gastric cancer (1). Blood transfusion (BTF) is frequently used as a treatment measure for gastric cancer patients experiencing perioperative anemia or bleeding. Numerous studies have explored the impact of perioperative BTF on postoperative complications and the prognosis of gastric cancer patients, yet the findings remain contentious (2-5). Moreover, prior research has highlighted that elderly patients with gastric cancer exhibit distinct clinical characteristics (6,7). Nevertheless, there is a scarcity of studies analyzing the influence of perioperative BTF on postoperative complications and prognosis in elderly patients with gastric cancer. Against this backdrop, the present study aimed to investigate this influence by retrospectively examining the clinical data of 1,666 elderly patients with gastric cancer admitted to our hospital who met the eligibility criteria. The findings are detailed below. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/ article/view/10.21037/jgo-23-906/rc).

Methods

Materials

The clinical data of gastric cancer patients who underwent radical surgery from October 2013 to October 2021 at the Department of Gastroenterology, Xijing Hospital were

Highlight box

Key findings

• Perioperative blood transfusion (BTF) was not an independent risk factor affecting the prognosis of elderly patients who underwent radical gastrectomy and had no significant effect on surgical complications except fever.

What is known and what is new?

- The effect of perioperative BTF on postoperative complications and prognosis in gastric cancer patients is still controversial, and there are few relevant reports on elderly patients.
- We found that perioperative BTF may have no significant effect on surgical complications and prognosis of elderly patients with gastric cancer.

What is the implication, and what should change now?

• Perioperative BTF may be feasible in elderly patients undergoing radical gastrectomy.

retrospectively collected.

To be eligible for inclusion in this study, the patients had to meet the following criteria: (I) be aged ≥ 60 years; (II) have been pathologically diagnosed with gastric adenocarcinoma; (III) have no distant metastasis in preoperative examinations; (IV) have undergone radical gastrectomy (R0 resection and D2 lymph node dissection); and (V) have complete clinical and follow-up data.

Patients were excluded from the study if they met any of the following exclusion criteria: (I) had a history of gastric surgery; (II) had a history of other malignancies; (III) died during the perioperative period; (IV) had a history of BTFs within 6 months before the surgery; and/or (V) had undergone emergency surgery. The flow chart of this study is shown in *Figure 1*.

Study methods

General pathological data

The following general pathological data were collected: sex, site and size of the tumor, extent of gastrectomy, degree of differentiation, T stage, N stage, tumor-node-metastasis (TNM) stage, preoperative hemoglobin (Hb) levels, intraoperative blood loss, perioperative BTF data, and complications in the immediate postoperative period (i.e., \leq 30 days post-surgery), including fever (defined as axillary temperature exceeding 37.3 °C), pulmonary infections, incision infections, anastomotic leakage, chylous leakage, pleural effusion, gastroparesis, intestinal obstruction, and abdominal infections.

The tumor sites and surgical methods were determined in accordance with the Japanese gastric cancer treatment guidelines 2014 (8), and pathological staging was performed according to the 7th edition of the TNM staging system for gastric cancer set by the Union for International Cancer Control (UICC) (9). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Xijing Hospital (No. KY20222190-C-1), and informed consent was obtained from all the patients.

Follow-up

Postoperative follow-up was carried out through outpatient review, telephone calls, and other forms of communication. The patients were followed-up every 3 months in the first postoperative year and every 6 months from the second year onwards. The endpoint was defined as death. The median follow-up time for patients overall was



Figure 1 Flow chart of data sources and screening of cases.

51 (range, 3.8–75.3) months.

Effect analyses of perioperative BTF on postoperative complications and prognosis

Based on whether the patients received a BTF (erythrocytes or whole blood) during the perioperative period, they were stratified into the BTF group and the non-BTF group. The immediate (≤30 days post-surgery) postoperative complications and the long-term (>30 days post-surgery) prognosis of the patients of the two groups were compared. Next, univariate and multivariate analyses were conducted to ascertain whether perioperative BTF was an independent risk factor associated with postoperative prognosis. Finally, further analyses based on the stratification of tumor stages (stage I/II/III) and transfusion time points (preoperative/ intraoperative/postoperative) were performed to determine the effect of perioperative BTF on patient prognosis.

Statistical methods

The statistical analyses were conducted using the Statistical Package for Social Science (SPSS) version 24.0 for Windows (IBM, Chicago, IL, USA). The χ^2 test was used for intergroup comparisons of the enumeration data; the Kaplan-Meier method was used for survival curve plotting; the log-rank test was used for intergroup comparisons of the survival rates; and the Cox regression model was used for the multivariate survival analysis. Differences were

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considered to be statistically significant at P<0.05.

Results

Intergroup comparison of clinical data

A total of 1,666 patients (male, n=1,357; female, n=309) were included in the study. The median age of the patients was 66 (range, 60–86) years. Among the patients, 1,255 (75.3%) were assigned to the non-BTF group and 411 (24.7%) were assigned to the BTF group. Additionally, 32 (1.9%) patients had Hb levels <70 g/L, 216 (13.0%) had Hb levels ranging from 70 to 100 g/L, and 1,418 (85.1%) had Hb levels >100 g/L. As *Table 1* shows, there were statistically significant differences between the two groups in terms of sex, site and size of the tumor, extent of gastrectomy, degree of differentiation, T stage, N stage, TNM stage, preoperative anemia, and intraoperative blood loss (P<0.05).

Effect of perioperative BTF on postoperative complications in elderly patients with gastric cancer

The incidence rates of postoperative complications of the patients in the non-BTF and BTF groups were 24.6% (309/1,255) and 43.8% (180/411), respectively, and the incidence rates of non-surgery-related complications of the patients in the two groups were 20.4% (256/1,255) and 37.2% (153/411), respectively. The differences

Liu et al. BTF in elderly patients who underwent radical gastrectomy

Table 1 Comparison of the clinicopathological characteristics of patients with perioperative BTF and without perioperative BTF

Characteristics	Non-BTF (n=1,255)	BTF (n=411)	χ^2 value	P value
Sex			7.532	0.006
Male	1,041 (82.9)	316 (76.9)		
Female	214 (17.1)	95 (23.1)		
Tumor location			8.950	0.03
Upper third	517 (41.2)	139 (33.8)		
Middle third	189 (15.1)	60 (14.6)		
Lower third	454 (36.2)	171 (41.6)		
Two thirds or more	95 (7.6)	41 (10.0)		
Tumor size (cm)			39.747	<0.001
<5	692 (55.1)	153 (37.2)		
≥5	563 (44.9)	258 (62.8)		
Resection type			10.755	0.005
Proximal	190 (15.1)	36 (8.8)		
Distal	434 (34.6)	152 (37.0)		
Total	631 (50.3)	223 (54.3)		
Differentiation status			9.789	0.02
Well	164 (13.1)	31 (7.5)		
Moderately	386 (30.8)	141 (34.3)		
Poorly	657 (52.4)	225 (54.7)		
Mucinous	48 (3.8)	14 (3.4)		
T stage			42.714	<0.001
T1	278 (22.2)	38 (9.2)		
T2	190 (15.1)	58 (14.1)		
Т3	410 (32.7)	189 (46.0)		
T4	377 (30.0)	126 (30.7)		
N stage			11.218	0.01
N0	519 (41.4)	137 (33.3)		
N1	200 (15.9)	62 (15.1)		
N2	223 (17.8)	82 (20.0)		
N3	313 (24.9)	130 (31.6)		
TNM stage			24.829	<0.001
I	368 (29.3)	70 (17.0)		
II	334 (26.6)	120 (29.2)		
III	553 (44.1)	221 (53.8)		
Preoperative Hb level (g/dL)			319.909	<0.001
<120	303 (24.1)	300 (73.0)		
≥120	952 (75.9)	111 (27.0)		
Intraoperative blood loss (mL)			95.793	<0.001
<300	1,030 (82.1)	240 (58.4)		
≥300	225 (17.9)	171 (41.6)		

Data are presented as n (%). BTF, blood transfusion; TNM, tumor-node-metastasis; Hb, hemoglobin.

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Variables	Non-BTF (n=1,255)	BTF (n=411)	χ^2 value	P value
Total complications	309 (24.6)	180 (43.8)	27.992	<0.001
Non-operation-related complications	256 (20.4)	153 (37.2)	26.922	<0.001
Fever	193 (15.4)	130 (31.6)	52.321	<0.001
Pneumonia	52 (4.1)	19 (4.6)	0.174	0.68
Pleural effusion	11 (0.9)	4 (1.0)	0.032	0.86
Operation related complications	53 (4.2)	27 (6.6)	3.349	0.07
lleus	17 (1.4)	9 (2.2)	1.406	0.24
Anastomosis leakage	13 (1.0)	7 (1.7)	1.487	0.48
Wound infection	8 (0.6)	2 (0.5)	0.118	0.73
Chyle leakage	7 (0.6)	4 (1.0)	0.815	0.37
Abdominal infection	5 (0.4)	4 (1.0)	1.904	0.17
Gastric stasis	3 (0.2)	1 (0.2)	<0.001	0.99

Table 2 Comparison of postoperative complications between BTF and non-BTF groups

Data are presented as n (%). BTF, blood transfusion.



Figure 2 OS of patients stratified by BTF group and non-BTF group. BTF, blood transfusion; OS, overall survival.

were statistically significant (P<0.001). Among all the complications, the incidence of postoperative fever of patients in the BTF group (31.6%) was significantly higher than that of patients in the non-BTF group (15.4%), and the difference was statistically significant (P<0.001). However, no statistically significant differences were observed between the two groups in terms of the incidences of postoperative surgery-related complications (i.e., intestinal obstruction, anastomotic leakage, incision

infections, chylous leakage, abdominal infections, and gastroparesis), respiratory infections, and pleural effusion (P>0.05). The above findings are outlined in *Table 2*.

Effect of perioperative BTF on postoperative survival in elderly patients with gastric cancer

As *Figure 2* shows, the Kaplan-Meier survival curve revealed that the postoperative overall survival (OS) of the patients in the non-BTF group was superior to that of the patients in the BTF group (3-year OS rates: 70.1% *vs.* 53.5%), and the difference was statistically significant (P<0.001). The univariate analysis revealed that the site and size of the tumor, extent of gastrectomy, degree of tumor differentiation, T stage, N stage, TNM stage, preoperative Hb levels, intraoperative blood loss, and perioperative BTF (P<0.001) were risk factors affecting the prognosis of elderly patients with gastric cancer. However, according to the further multivariate analysis, only tumor size, T stage, N stage, and intraoperative blood loss were independent risk factors affecting the prognosis of elderly patients with gastric cancer. The above findings are set out in *Table 3*.

As *Figure 3* shows, the stratified analysis demonstrated that patients with stage III tumors in the BTF group had a significantly inferior prognosis compared to that of those in the non-BTF group (3-year OS rates: 33.7% *vs.* 47.9%), and the difference was statistically significant (P<0.001).

Liu et al. BTF in elderly patients who underwent radical gastrectomy

Table 3 Univariate and multivariate analysis of the risk factors for the prognosis of patients

.	N	Univariate analysis		Multivariate analysis		
Characteristics		3-year survival rate (%)	P value	HR (95% CI)	P value	
Sex			0.42			
Male	1,357	66.2				
Female	309	65.1				
Tumor location			0.36			
Upper third	656	62.7				
Middle third	249	68.9				
Lower third	625	72.2				
Two thirds or more	136	45.7				
Tumor size (cm)			<0.001	1.416 (1.183–1.696)	< 0.001	
<5	845	80.3				
≥5	821	51.6				
Resection type			<0.001	1.011 (0.894–1.144)	0.86	
Proximal	226	74.5				
Distal	586	75.2				
Total	854	57.1				
Differentiation status			<0.001	0.955 (0.846–1.077)	0.45	
Well	195	86.9				
Moderately	527	70.2				
Poorly	882	58.9				
Mucinous	62	61.0				
T stage			<0.001	1.567 (1.353–1.815)	< 0.001	
T1	316	93.7				
T2	248	82.4				
Т3	599	65.5				
T4	503	41.4				
N stage			<0.001	1.583 (1.394–1.798)	<0.001	
NO	656	87.6				
N1	262	75.5				
N2	305	56.2				
N3	443	35.6				
TNM stage			<0.001			
I	438	93.2				
II	454	78.1				
III	774	43.9				
Preoperative Hb level (g/dL)			<0.001	0.901 (0.754–1.077)	0.25	
<120	603	57.4				
≥120	1,063	70.2				

Table 3 (continued)

Characteristics	N	Univariate analysis		Multivariate analysis		
	IN	3-year survival rate (%)	P value	HR (95% CI)	P value	
Intraoperative blood loss	s (mL)		<0.001	1.360 (1.146–1.615)	<0.001	
<300	1,270	69.8				
≥300	396	54.0				
Perioperative BTF			<0.001	1.178 (0.971–1.428)	0.10	
No	1,255	70.1				
Yes	411	53.5				

Table 3 (continued)

HR, hazard ratio; CI, confidence interval; BTF, blood transfusion; Hb, hemoglobin.



Figure 3 Comparison of OS according to perioperative BTF in the same tumor stage. TNM, tumor-node-metastasis; BTF, blood transfusion; OS, overall survival.

Conversely, in patients with stage I/II tumors, there was no statistically significant difference in prognosis between the two groups (3-year OS rates for stage I patients: 94.0% vs. 93.6; stage II patients: 80.7% vs. 70.7%; P>0.05). The factors affecting prognosis in patients with stage III tumors were further analyzed, and the results are set out in *Table 4*. The univariate analysis indicated that perioperative BTF was one of the risk factors affecting prognosis (P<0.001), but the multivariate analysis demonstrated that it was not an independent risk factor affecting prognosis (P=0.12).

Effect of perioperative BTF at various time points on postoperative survival in elderly patients with gastric cancer

The postoperative survival of patients who were transfused only preoperatively (n=41), intraoperatively (n=123), or postoperatively (n=130) was compared. As *Figure 4* shows, the postoperative 3-year OS rates were 57.2%, 51.1%, and 54.6% respectively, and the postoperative 5-year OS rates were 39.1%, 42.9%, and 46.1% respectively. The differences were not statistically significant (P=0.87).

Discussion

It has been reported that about 20% of patients undergoing gastrectomy need a BTF due to perioperative anemia or intraoperative bleeding (10). Multiple studies have revealed the effect of BTF on the postoperative complications and the prognosis of gastric cancer patients, but the conclusions remain controversial. Squires *et al.* (11) analyzed 765 gastric cancer patients at seven institutions from the United States Gastric Cancer Collaborative and discovered that the postoperative disease-free survival (DFS) and OS rates were significantly reduced in the patients who received

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Variables	Regression coefficient	Standard error	Wald χ^2	P value	HR (95% CI)	
Tumor size	0.338	0.111	9.201	0.002	1.402 (1.127–1.743)	
Resection type	0.042	0.078	0.286	0.59	1.043 (0.894–1.216)	
T stage	0.458	0.089	26.673	<0.001	1.582 (1.329–1.882)	
N stage	0.474	0.077	37.786	<0.001	1.606 (1.381–1.868)	
Preoperative Hb level	-0.115	0.105	1.196	0.27	0.891 (0.725–1.095)	
Intraoperative blood loss	0.331	0.101	10.756	<0.001	1.392 (1.142–1.696)	
Perioperative BTF	0.174	0.113	2.394	0.12	1.191 (0.955–1.485)	

Table 4 Multivariate analysis of prognostic factors in elderly patients with stage III gastric cancer

HR, hazard ratio; CI, confidence interval; BTF, blood transfusion; Hb, hemoglobin.



Figure 4 OS of patients compared by preoperative, intraoperative, and postoperative BTF. BTF, blood transfusion; OS, overall survival.

perioperative BTFs. Two meta-analysis studies have shown that perioperative BTF is associated with negative survival effects (in terms of OS, DFS, and disease-specific survival) and a higher incidence of perioperative complications in gastric cancer patients (12,13). Another study of 927 patients from six Italian study centers revealed that the effect of BTF on the postoperative 5-year survival rate was not significant in gastric cancer patients (14). However, few studies have examined the effect of perioperative BTF on complications and prognosis after radical gastrectomy in elderly patients. To our knowledge, the present study, which analyzed the clinical data of 1,666 elderly patients who had undergone gastrectomy, is the largest singlecenter study to examine the effect of perioperative BTF on the postoperative complications and prognosis of elderly patients with gastric cancer.

The baseline data analysis in this study showed that patients in the BTF group were in more advanced tumor stages, and that more of them had preoperative anemia, overall tumor sizes ≥ 5 cm, and intraoperative blood loss volumes ≥ 300 mL compared with patients in the non-BTF group. The findings are consistent with the results of multiple previous studies (2-5).

Controversies still exist regarding the relationship between perioperative BTF and postoperative complications in gastric cancer patients. It has been found that BTF might elevate the incidence of perioperative complications among gastric cancer patients (12,15). Conversely, Kouyoumdjian et al.'s study of 9,936 gastric cancer patients showed that perioperative BTF might lower the incidence of postoperative complications and the mortality rate of patients with severe anemia (hematocrit <29) (3). Xiao et al. reported that BTF was an independent risk factor for postoperative infections in gastric cancer patients (10). However, a previous study showed that the incidence rates of postoperative infectious complications were similar between the perioperative BTF and non-BTF groups after propensity-score matching was used to diminish the intergroup differences in clinical tumor characteristics and surgery-related factors (16). In the present study, the overall incidence of postoperative complications in the BTF group (43.8%) was significantly higher than that in the non-BTF group (24.6%), which was mainly due to the significantly increased incidence of postoperative fever in the BTF group (31.6%) compared with that in the non-BTF group (15.4%), as shown by further analyses. However, no significant intergroup differences were observed in the incidences of other complications. The findings suggest that BTF did not

elevate the incidences of perioperative complications (other than fever) among elderly patients with gastric cancer. Additionally, it has been reported that fever is the most common complication of BTF and might be associated with the immune response (17).

Tumor staging is a decisive factor affecting the prognosis of gastric cancer patients. However, controversy continues as to whether BTF affects the prognosis of gastric cancer patients. A retrospective study of 1,581 patients by Liu et al. confirmed that perioperative BTF was associated with the poor prognosis of patients with stage III gastric cancer (18). Kanda et al. showed that BTF was also an independent risk factor for a poor prognosis in patients with stage II/III gastric cancer (19). Further, a meta-analysis of 18 studies showed that perioperative BTF was related to a poor prognosis in patients undergoing gastrectomy (20). However, Gong et al. pointed out that the literature included in this meta-analysis study was insufficient and the results were partially contradictory (21). Meanwhile, Hyung et al. revealed that BTF had a non-significant effect on the postoperative survival rates of patients with stage I/II gastric cancer (22). For patients with stage III gastric cancer, Yamashita et al. showed that BTF had no effect on their postoperative survival (23). Zhou et al. carried out an analysis stratified by tumor stages (stage I/II/III) of 605 gastric cancer patients, and found no differences in the postoperative survival rates among the patients in different stages in both the non-BTF and BTF groups, which suggests that BTF was not an independent risk factor affecting the postoperative survival of gastric cancer patients (24).

In the present study, the postoperative 3-year OS rate in patients in the BTF group was significantly lower than that in patients in the non-BTF group, and the further analyses stratified by tumor stages indicated that BTF had a significant effect on prognosis in patients with stage III gastric cancer but not in patients with stage I/II gastric cancer. These findings are identical to the results reported by Xue et al. (25) However, our multivariate analysis demonstrated that BTF was not an independent risk factor affecting the prognosis of gastric cancer patients in all the three stages, and that it might have been closely associated with the more advanced tumor stages and the greater intraoperative bleeding in patients in the BTF group. Further, Rausei et al. also reported that BTF was not an independent risk factor affecting the prognosis of gastric cancer patients but was a confounder that was considerably influenced by other variables (26). In a study of 2,905 patients with stage II/III gastric cancer, Song et al.

found no significant correlation between perioperative BTF and the long-term survival of the patients after the intergroup differences in clinical tumor characteristics and surgery-related factors were diminished using propensity score matching (2). These findings are consistent with those of Xiao *et al.* and Cui *et al.* (16,27), and similar to the conclusions drawn by studies on other cancers (28,29).

In addition, the definition of perioperative BTF is also a potential factor that could have led to the differences reported by various studies, as the definition may encompass different transfusion time points, transfused volumes, and transfused components. In terms of transfusion time points, the majority of studies have included patients who received BTF 1 or 2 weeks preoperatively, and 1 or 2 weeks or even 1 month postoperatively (19,24), while only one study included patients undergoing intraoperative and/ or postoperative BTF (11). Xue *et al.* noted that gastric cancer patients who underwent BTF intraoperatively exhibited a significantly inferior prognosis compared with that of patients who underwent BTFs preoperatively or postoperatively (25).

In relation to transfused volumes, a previous study reported a negative correlation between transfused volumes and patient prognosis (22). Conversely, Xue *et al.* stratified gastric cancer patients into three groups based on the volumes of perioperative red blood cell transfusion (<2, 2–4, and >4 U), and found no significant difference in the postoperative prognosis among the patients across all the groups (25).

In relation to the transfused components, Dhar et al. reported that patients who were only transfused with concentrated erythrocytes had notably higher survival rates than those who were transfused with other blood products (30). van Hilten et al. showed that in patients in the erythrocyte group who underwent leucocyte-filtered transfusion, the average hospitalization duration was 2.4 days shorter and the incidence of multi-organ failure was 30% lower than that of patients in the non-filtration group, but the difference in the mortality rates between the two groups was not significant (31). Additionally, another study found no statistically significant differences in the mortality and tumor recurrence rates between filtration and nonfiltration groups (32). In the present study, perioperative BTF referred to the transfusion of erythrocytes from admission to discharge (typically 3 days preoperatively to 14 days postoperatively). Finally, no significant difference was discovered in the effect of preoperative, intraoperative, and postoperative BTFs on the prognosis of elderly patients

564

with gastric cancer, which is consistent with the findings of Song *et al.* (2) obtained in the study on patients with stage II/III gastric cancer.

This study had a number of limitations: (I) it was a single-center retrospective study; and (II) some of the patients included received platelet or plasma transfusions concurrently, and the effects of transfused volumes and components on prognosis were not further investigated through a stratified analysis.

Conclusions

Perioperative BTF may elevate the incidence of postoperative fever in elderly patients with gastric cancer, but it has no significant effect on other complications. Additionally, BTF is not an independent risk factor affecting the postoperative prognosis of elderly patients with gastric cancer. As the definitions of perioperative BTF vary among hospitals and physicians, multi-center studies with larger sample sizes need to be conducted to obtain higher-level evidence.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Xijing Hospital (No. KY20222190-C-1), and informed consent was obtained from all the patients.

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