

ORIGINAL ARTICLE

Perioperative blood transfusion is one of the factors that affect the prognosis of gastric cancer

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Summary

Purpose: To demonstrate the potential significance of perioperative blood transfusion on the prognosis of gastric cancer.

Methods: Data from 234 patients who were subjected to radical gastrectomy in our hospital were obtained and retrospectively analyzed. Patients' age, gender, preoperative anemia, tumor size, location, invasion depth, lymph node metastasis, TNM stage, presence or absence of blood transfusion and blood transfusion volume were observed and analyzed.

Results: The difference of tumor recurrence in patients whose blood transfusion volume was greater than 2U was significant ($p < 0.001$). The tumor recurrence in patients whose blood transfusion was less than 2U was significantly shorter than in those whose transfusion volume was greater than 4U ($p = 0.03$). The survival in the blood transfusion group was significantly lower in comparison with the non-

blood transfusion group ($p = 0.002$). The survival of transfusion group in TNM stage III and IV was significantly shorter than that in non-transfusion group ($p = 0.03$). Statistical significance was found in survival between the transfusion group and non-transfusion group when the tumor size was less than 5 cm and greater than 5 cm ($p = 0.006$, $p = 0.04$, respectively).

Conclusions: Perioperative transfusion is one of the factors for predicting the prognosis of postoperative gastric cancer patients, and the larger the perioperative transfusion, the shorter the tumor recurrence, the worse the prognosis. Therefore, it is of great significance reducing the intraoperative blood loss and strict controlling blood transfusion indications.

Key words: gastric cancer, perioperative transfusion, recurrence, survival time

Introduction

Gastric cancer is a rather common malignant tumor. It ranks second in the global cancer death. Patients with gastric cancer often need perioperative transfusion due to anemia caused by bleeding, malnutrition and chronic diseases [1]. However, there is a risk connected with blood transfusions, especially in cancer patients, because it can lead to immunosuppression, thus negatively affecting

their prognosis [2]. In 1982, Burrow et al. [3] first proposed perioperative transfusion in cancer patients after colon cancer surgery. In 1987, Kaneda et al. [4] studied 231 patients with gastric cancer and found that blood transfusion attributed significantly to poor patient outcome. One study pointed out that perioperative transfusion has a certain link with poor prognosis [5], while others have

reported no significant relationship [6-10]. Nowadays, with the improvement and advancement of clinical surgical techniques, the risk of bleeding during the operation has gradually reduced, and the proportion of patients requiring blood transfusion has also gradually reduced. However, some patients still require blood transfusion due to malnutrition and related bleeding during surgery. In recent years, there is still some controversy about whether the perioperative transfusion will adversely affect the gastric cancer patients after surgery.

The current study considered that poor outcomes after surgery resulted from perioperative transfusion and was due to immunosuppressive and inflammatory changes caused by blood transfusion [11]. However, relative research is still lacking. Herein, we tried to clarify whether perioperative transfusion was related to the prognosis of gastric cancer patients. In addition, we also evaluated other important clinical and oncological features, including age, gender, tumor site, tumor size, anemia, invasion depth, lymph node metastasis and TNM staging.

Methods

Study subjects

The clinical data of 234 patients who underwent radical gastrectomy in the First People's Hospital of Lianyungang from July 2010 to July 2012 were retrospectively analyzed. Among them, 159 were males and 75 females, with average age 65 years (range 31-82). All patients were pathologically diagnosed with primary gastric cancer. The collected data included patient age, gender, preoperative anemia, tumor size, tumor location, invasion depth, lymph node metastasis, TNM staging (7th Edn [12]), presence or absence of blood transfusion, and blood transfusion volume. This study was approved by the Ethics Committee of the First People's Hospital of Lianyungang and all patients provided signed informed consent. Two hundred and twenty of the study participants were successfully followed-up (follow-up rate 90.6%) for 60 months. The follow-up results were expressed as number of survival months, until the patient died or follow-up time reached 60 months.

Statistics

SPSS 22.0 software package was used for statistical analyses and all measurement indicators were described as mean±standard deviation. The hypothesis test used two independent series of t-test. Percent data between groups were analyzed using the χ^2 test. Kaplan-Meier method was used to construct survival curves and log-rank test was used to compare differences between groups. Multivariate logistic regression analysis was performed to determine independent prognostic factors. A p value <0.05 indicated the difference was statistically significant (* p<0.05, ** p<0.01, *** p<0.001).

Results

General data of patients

Of the 234 enrolled patients, 119 (82 males and 37 females) were included in the treatment group and 115 (77 males and 38 females) in the control group. We did not observe significant differences in gender, age and tumor location between the two groups. There were significant differences in tumor size, anemia, invasion depth, lymph node metastasis and TNM staging compared in the two groups (p<0.05). Detailed information is listed in Table 1.

Blood transfusion and tumor recurrence time

According to the amount of blood transfusion, patients were assigned into <2U, 2-4U and >4U groups based on perioperative transfusion. After 5 years of follow-up, there were 64 (55.7%) cases of tumor recurrence in the non-transfused group and 83 (69.7%) in the transfusion group. There were 23 (27.7%) cases in the <2U group, 36 (43.4%) cases in the 2-4U group and 24 (28.9%) cases in the >4U group. The results illustrated that the time to recurrence in the non-transfused group was shorter than that of the above three groups, with statistically significant difference (p=0.04, p<0.001, p<0.001, respectively), and when the transfusion volume was >2U, the difference of time to recurrence was significant (p<0.001). When compared in the three groups, no significant difference was

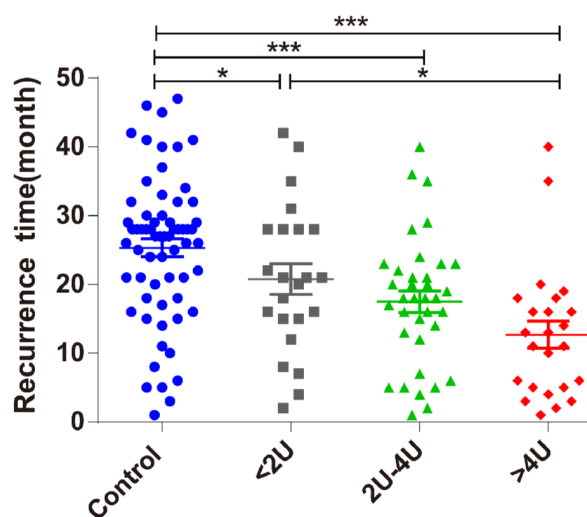


Figure 1. The recurrence time was conversely related with blood transfusion volume. The time to recurrence in the non-transfused group was shorter than that of above three groups. When the transfusion volume was >2U, the difference of time to recurrence was significant. When compared in the three groups, no significant difference was found in time to recurrence between <2U and 2-4U group. The time to recurrence in the <2U group was significantly shorter than in the 4U group. *p<0.05, ***p<0.001.

found in time to recurrence between <2U and 2-4U group ($p>0.05$). However, the time to recurrence in the <2U group was significantly shorter than in the >4U group ($p=0.03$). The above results indicated that the larger the perioperative transfusion, the shorter the time to recurrence and the worse the prognosis. Relative results are presented in Figure 1.

Blood transfusion and survival time

Our data demonstrated significant difference in survival between the transfusion group and the non-transfusion group, with lower survival in the transfusion group ($p=0.002$), as shown in Figure 2A. Analyzing the relationship between TNM staging and perioperative transfusion we found that the survival time in the TNM III+IV transfusion

groups was significantly shorter compared with the non-transfusion group ($p=0.03$), however, no significant difference between the two groups in TNM I+II transfusion group was observed ($p>0.05$). Significant differences in the survival time were registered between the non-transfused group and the transfused group when the tumor size was < 5 cm and >5 cm ($p=0.006$, $p=0.04$, respectively). Detailed results are shown in Figure 2.

Influence of other variables on the relationship between perioperative transfusion and survival

Multivariate survival analysis indicated that age, invasion depth, lymph node metastasis, TNM staging and perioperative transfusion were independent prognostic factors in gastric cancer patients as shown in Table 2.

Table 1. General patient data

	Transfusion group n (%)	Non-transfusion group n (%)	p value
Gender			0.75
Male	82 (68.9)	77 (67.0)	
Female	37 (31.1)	38 (33.0)	
Age, years, mean±SD	53.2±6.73	50.3±7.68	0.12
Preoperative anemia			<0.001
Yes	79 (66.4)	21 (18.3)	
No	40 (33.6)	94 (81.7)	
Tumor location			
Cardia and fundus ventriculi	16 (13.4)	14 (12.2)	0.77
Corpora ventriculi	41 (34.5)	46 (40.0)	0.38
Sinuses ventriculi	62 (52.1)	55 (47.8)	0.51
Tumor size, cm			0.02
< 5	56 (47.1)	72 (62.6)	
> 5	63 (52.9)	43 (37.4)	
Invasion depth (T stage)			
T ₁	6 (5.1)	14 (12.2)	0.05
T ₂	20 (16.8)	27 (23.5)	0.20
T ₃	78 (65.5)	70 (60.8)	0.46
T ₄	15 (12.6)	4 (3.5)	0.02
Lymph node metastasis (N stage)			
N ₀	25 (21.0)	38 (33.1)	0.04
N ₁	46 (38.7)	48 (41.7)	0.63
N ₂	30 (25.2)	22 (19.1)	0.26
N ₃	18 (15.1)	7 (6.1)	0.03
TNM stage			
I	12 (10.1)	28 (24.3)	<0.01
II	26 (21.8)	40 (34.8)	0.03
III	55 (46.2)	38 (33.1)	0.04
IV	26 (21.9)	9 (7.8)	<0.01

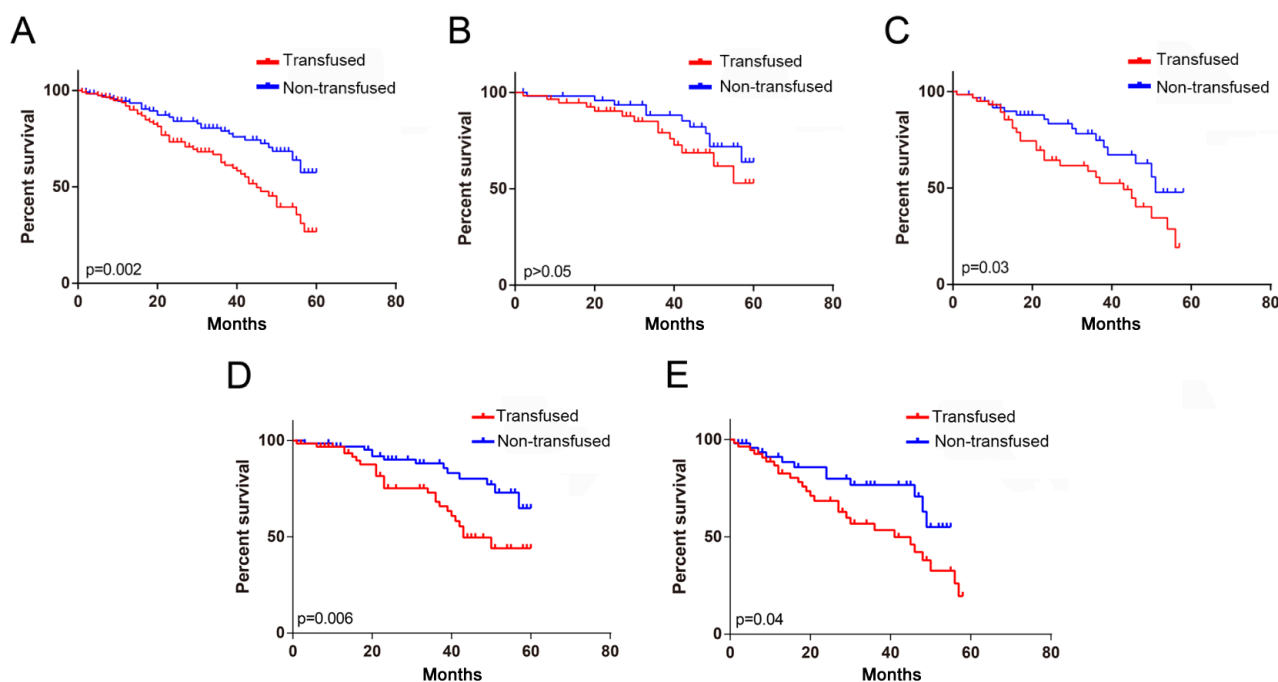


Figure 2. The relationship between blood transfusion and survival. **A:** Perioperative transfusion reduced the postoperative survival time of gastric cancer patients. **B:** The survival in TNM I and II transfusion group showed no significant difference between the two groups. **C:** The survival in TNM III and IV transfusion group was significantly shorter compared with the non-transfusion group. **D:** When the tumor size was <5 cm, the survival time of the transfusion group was significantly shorter. **E:** When the tumor size was >5 cm, the survival time of the transfusion group was significantly shorter.

Table 2. Multivariate logistic regression analysis of factors affecting postoperative survival

Factors	B	SE	Wald	OR	95%CI	p value
Perioperative transfusion	1.301	0.346	14.111	3.673	2.017-4.812	0.001
Age	0.583	0.436	1.821	1.793	2.846-3.965	0.017
Invasion depth	0.577	0.204	7.996	1.782	3.293-4.164	0.004
Lymph node metastasis	0.757	0.293	6.563	2.130	1.130-3.753	0.012
TNM stage	0.324	0.142	4.482	1.339	1.213-2.136	0.023

Discussion

With the continuous development of diagnostic and medical technology, the early diagnosis of gastric cancer has been significantly improved. Endoscopic resection, anticancer chemotherapy, surgical resection and other treatment methods are gradually being used in the treatment of patients with gastric cancer to improve the prognosis. Despite the surgical removal of cancer, the early postoperative recurrence rate is high, and prognosis and long-term survival rate are poor [13]. Therefore, the study of risk factors affecting the prognosis of gastric cancer patients is the focus of intense clinical research.

Gastric cancer patients present preoperative anemia due to chronic and long-term decreased consumption of food or chronic bleeding caused by the tumor. These patients may also present re-

duced blood volume because gastric vessels are rich and lymph node dissection can easily lead to massive bleeding. Meanwhile, postoperative radiotherapy and chemotherapy could lead to anemia, and all of the above require perioperative transfusion. However, recent articles pointed out that perioperative transfusion affect the prognosis of patients. Squires at al. analyzed patients undergoing resection of gastric cancer in 7 gastric cancer institutions in USA, and concluded that perioperative transfusion is an independent prognostic and recurrence risk factor of gastric cancer [14]. Similarly, Mizuno et al. retrospectively analyzed 203 cases of gastric cancer patients subjected to radical resection, both in TNM II,III without preoperative blood transfusion. The patients were assigned into intraoperative blood transfusion group and intraoperative non-transfusion group and the authors concluded that intraoperative blood transfusion

was independent risk factor of prognosis [15]. Kanda et al. [16] also believed that blood transfusion is an independent prognostic risk factor, and intraoperative blood transfusion is not good for prognosis. Our results were similar to the above studies.

The present study included 234 patients whose 5-year survival was retrospectively studied. The results indicated that perioperative transfusion was a risk factor that affected the disease prognosis (Figure 2A). At the same time, patients were assigned into three groups based on the different blood transfusion volume. What we found was that the larger the blood transfusion volume, the worse the prognosis of patients and the shorter the tumor free survival. Multivariate logistic regression analysis demonstrated that age, invasion depth, lymph node metastasis, TNM staging and perioperative transfusion were all independent factors of prognosis in patients with gastric cancer. Therefore, this article stratified the value of perioperative transfusion in the prognosis of gastric cancer patients according to TNM staging and tumor size. Also, this study found that blood transfusion had a great impact on the prognosis of gastric cancer patients in TNM III and IV stages, but no significant difference in TNM I and II patients was observed (Figures 2B,2C). In terms of tumor size, blood transfusion had a negative prognostic effect with statistical differences (Figures 2D,2E). These results suggested that perioperative transfusion negatively affects the prognosis of gastric cancer.

However, some authors still consider that blood transfusion is not an independent prognostic risk factor for patients with gastric cancer, which

fundamentally negates the relationship between blood transfusion and prognosis [17,18]. However, some studies have suggested that blood transfusion suppresses the immune function and promotes tumor recurrence [19-23]. We also maintain that perioperative transfusion should be avoided in patients with gastric cancer.

In summary, perioperative transfusion is one of the prognostic factors of gastric cancer, and the larger the perioperative transfusion, the shorter the time to recurrence and the worse the prognosis. Therefore, it is of great significance to reduce the intraoperative blood loss in order to reduce the blood transfusion indication.

Conclusions

Perioperative blood transfusion is one of the factors predicting the prognosis of postoperative gastric cancer patients, and the larger the perioperative transfusion, the shorter the tumor recurrence and the worse the prognosis. Therefore, it is of great significance to reduce the intraoperative blood loss.

Acknowledgement

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Conflict of interests

The authors declare no conflict of interests.

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