Research Paper

Effect of Perioperative Blood Transfusion on the Survival of Gastric Cancer Patients Undergoing Laparoscopic Gastrectomy

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Femoral head necrosis is a mobility disorder and till now no satisfactory solution has been reported. The principal contributing factor in the pathogenesis of the disease is insufficient blood supply to the femoral head resulting in necrosis of the femoral head. Various preventive measures required to treat femoral head necrosis include revascularization, adequate supply of osteogenic cells and establishing enough strength to avoid collapse. Among all, cell transplantation therapy is considered the most favourable treatment strategy for femoral head necrosis. However, the results merely depend on the etiology and the clinical stage of femoral head necrosis. Thus, it is better to make a treatment plan according to the epidemiology, disease status and stage. The main objective of this communication is to study the treatment of femoral head necrosis with cell replacement therapy and also its effects by focusing on the disease stages.

Key words: Perioperative blood transfusion, laparoscopic gastrectomy, gastric cancer, overall survival, disease free survival

Gastric cancer (GC) is the fourth most common cancer in the world, which is also the second leading cause of cancer death in China. Its main clinical symptoms are abdominal pain, intestinal bleeding or intestinal obstruction necrosis, which is one of the diseases with high mortality at present. So far, the main treatment of GC has been radical gastrectomy. Because a large number of GC patients often have anaemic symptoms and gastrectomy+lymph node dissection sometimes leads to a large amount of blood loss during operation, which is easy to cause adverse reactions during operation, such as low immune function, electrolyte disorder and blood coagulation dysfunction, which brings great risk to the treatment of patients[1,2].

Therefore, blood transfusion (BTF) is a life-saving treatment in the radical resection of GC. Although the demand for BTF is decreasing due to the improvements in surgical techniques and perioperative care[3], many studies have shown that perioperative blood transfusion (PBT) is related to the decrease of overall survival (OS) and disease-free survival (DFS) in patients undergoing radical resection of GC[4-6]. Some studies have shown that there is a causal relationship and has an effect on the immune system, thereby enhancing immunosuppression[1,7,8]. In addition, studies have shown that there is no difference in long-term prognosis between patients undergoing laparoscopic radical gastrectomy and open radical gastrectomy[2,3,9-11]. However, compared with laparotomy, laparoscopic gastrectomy has a lower immunosuppressive rate, blood loss and requirement for blood transfusion[11-14].

However, other studies have suggested that BTF is a complex factor rather than a prognostic indicator because it is significantly affected by other factors. Therefore, the relationship between BTF and the prognosis of GC is still controversial. It is believed that the decline in the long-term survival rate of GC patients receiving BTF is not only caused by BTF, but other reasons might also be involved. It can also be related to the degree of the tumor and other prognostic factors

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related to BTF, such as advanced age, difficulty and duration of the operation. This study aims to investigate the risk factors of PBT and its effect on long-term prognosis in patients treated with laparoscopic radical gastrectomy.

MATERIALS AND METHODS

Patients:

All patients treated with laparoscopic gastrectomy in Taikang Xianlin Drum Tower hospital from December 2013 to December 2018 were included and divided into the non-transfusion group (n=58) and the blood transfusion group (n=45). All operations were performed by 2 senior surgeons. The patient's age, sex, body mass index, American Society of Anesthesia score, tumor location, tumor, node and metastasis (TNM) stage, conversion to open gastrectomy, postoperative mortality and morbidity in 30 d and pathological data were collected directly from medical records.

OS and DFS data were collected from the outpatient clinic and patient follow-up data. OS assessment is from the date of operation to the last follow-up or death of any cause. The DFS assessment is from the date of the operation to the time when the cancer relapses or when the patient dies from any cause.

PBT includes all blood transfusions on the day of the operation or 30 d during hospitalization after operation. Preoperative evaluation included superior gastrointestinal endoscopy, endoscopic ultrasonography, brain, chest and abdominal CT scans and abdominal ultrasound examination. Selected cases were scanned by positron emission computerized tomography (PECT) and bone scan if necessary.

The TNM staging of GC was performed according to the 8th edition of GC TNM staging system issued by the Union for International Cancer Control (IUAC) and American Joint Committee on Cancer (AJCC) in October 2016[15-18]. Perioperative mortality included deaths within 30 d after gastrectomy. The postoperative morbidity was classified according to the Clavien-Dindo classification[21-24], the main complications were divided into 3, 4 and 5 grades and the minor complications included 1 and 2 grades.

After discharge, patients were followed up every 3 mo in the first 2 y, every 6 mo in the following 3 y and every 6 mo or annually thereafter. Physical examination and routine haematological examinations were carried out during each follow-up. Abdominal CT or abdominal ultrasound and chest X-ray were re-examined 6 mo after the operation. Disease recurrence is defined as local or distant metastasis of cancer cells confirmed by radiation or pathology and the time of diagnosis is determined by the interval between surgery and the last follow-up. The last scheduled follow-up was August 2019. This is a retrospective study, which was approved by the institutional review committee of Taikang Xianlin Drum Tower hospital and the patients signed an informed consent form.

Statistical analysis:

SPSS 20.0 was used for statistical analysis. The normal distribution data are expressed as mean±standard deviation and the differences are analysed using independent t-test. The data of non-normal distribution were expressed as median and range and the differences were compared using the Mann-Whitney U test. Mann-Whitney U test was used to analyze the difference of semi-quantitative results. Where appropriate, chi-square test or Fisher accurate test was used to analyse the differences in qualitative results.

The survival rate was estimated by the Kaplan-Meier method and the significant difference was determined by the logarithmic rank test. Univariate analysis was used to determine and select the factors that had significant effects on OS and DFS ($p<0.10$), which were included in the multivariate Cox proportional risk regression model. The adjusted risk ratio (h) and the corresponding 95 % confidence level were used to calculate the confidence interval (CIs). $p<0.05$ is considered to be statistically significant.

RESULTS AND DISCUSSION

In this study, 103 patients treated with laparoscopic gastrectomy were included. Forty-five patients (43.7 %) received BTF on the day of gastrectomy or 30 d during hospitalization after the operation. Compared with patients without PBT, patients who received BTF usually have the characteristics of older age, low preoperative hemoglobin level, advanced cancer, multiple complications, high open radical gastrectomy rate and high incidence of complications within 30 d after the operation (Tables 1 and 2).

The median follow-up period was 38 mo and 5 patients (3 in the blood transfusion group and 2 in the non-transfusion group) lost at each time point. In patients receiving blood transfusions, both OS and DFS decreased significantly (figs. 1 and 2). The cancer stage and multiple complications were independent influencing factors of OS (Tables 3 and 4) and DFS

TABLE 1: CLINICAL AND PATHOLOGICAL FEATURES OF THE TWO GROUPS

Features	Non-transfusion group (n=58)	Blood transfusion group (n=45)	p value
Age (y)	55.71±11.84	54.98±11.10	0.516
Gender (male/female)	39:19	25:20	0.700
Preoperative hemoglobin level (g/l)(Range)	117 (81-158)	93 (74-148)	0.026
Numbers of complications			
0	36	29	0.465
1	14	8	1.000
2	7	5	1.000
≥3	1	3	0.031
ASA score			
I	36	34	0.687
II	19	9	0.731
III	3	2	1.000
Number of lymph node dissection	17 (15-29)	14 (16-27)	0.189
Residual tumor (R0/R1/R2)	58/0/0	45/0/0	1.000
Histodifferentiation			0.625
Differentiation	34	32	
Undifferentiation	24	13	
TNM staging			
I	24	2	0.000
II	18	24	0.086
III	16	19	0.000

TABLE 2: RESULTS OF SURGERY IN THE TWO GROUPS

	Non-transfusion group (n=58)	Blood transfusion group (n=45)	p value
Type of gastrectomy			0.661
Total gastrectomy	24	16	
Distal gastrectomy	34	29	
Open radical gastrectomy	12	10	0.004
Operation time, min (Range)	180 (140-290)	200 (160-280)	0.102
Estimated blood loss, ml (Range)	210 (160-490)	220 (180-440)	0.098
Postoperative residence time, d	10	13	0.078
30 d postoperative complications	19	13	0.002
Serious complications	4	2	0.879
Minor complications	15	11	

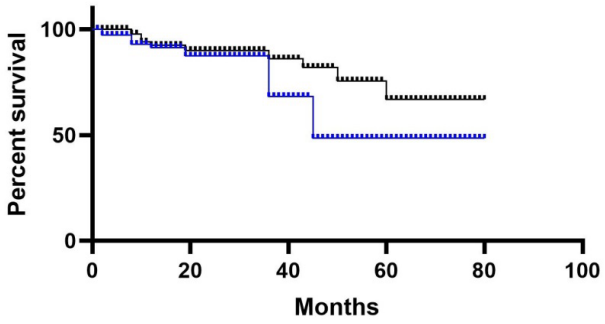

Fig. 1: OS curve of two groups of GC patients (—■—) Blood transfusion group, (—■—) Non blood transfusion group

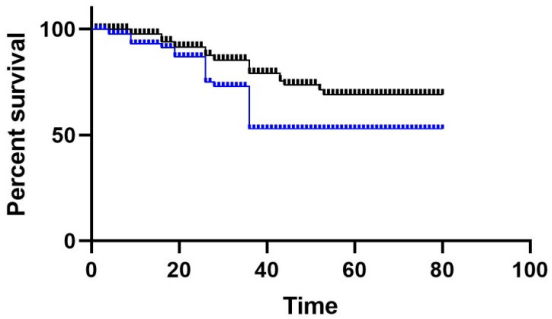

Fig. 2: DFS curve of two groups of GC patients (—■—) Blood transfusion group, (—■—) Non blood transfusion group

(Tables 5 and 6). Patients who received PBT did not find an independent association with a reduced risk of OS or DFS.

In this study, BTF was found to be related to low OS and DFS after laparoscopic radical gastrectomy. Patients who received BTF were of older age with

TABLE 3: UNIVARIATE ANALYSIS OF 5-YEAR OS

Variable	5-y OS (%)	p value
Age (y)		0.127
<65	55	
≥65	41	
Sex		0.122
Male	49	
Female	38	
ASA scores		0.128
I-II	51	
III	37	
Number of complications		0.032
No	59	
Yes	32	
Type of gastrectomy		0.128
Total gastrectomy	50	
Distal gastrectomy	42	
TNM staging		0.000
I-II	65	
III	32	
Histodifferentiation		0.205
Differentiation	46	
Undifferentiation	37	
Serious complications		0.054
Yes	54	
No	41	
PBT		0.040
Yes	48	
No	40	

TABLE 4: COX PROPORTIONAL RISK MODEL FOR OS

Variable	Risk coefficient R	p value
TNM staging (I-II VS III)	2.158 (1.269-4.870)	0.018
Number of complications (<2 VS ≥2)	2.510 (1.257-4.020)	0.021

low preoperative hemoglobin level, advanced cancer, multiple complications, high open radical gastrectomy rate and high incidence of complications. However, multivariate analysis did not find that BTF was an independent risk factor for re OS or DFS reduction. It has been previously reported that laparoscopic gastrectomy can reduce tissue injury and better protect immune function compared with open gastrectomy[7-10]. In theory, reducing tissue damage can reduce the effect of PBT on the immune system, thus reducing OS and DFS.

The amount of blood loss in laparoscopic surgery is usually lower than that in open gastrectomy. A decrease in the BTF rate is not the inevitable result of the reduction of blood loss. However, it is reported that laparoscopic gastrectomy can reduce the volume of PBT and the number of transfusion patients. In this study, the PBT rate was found to be relatively high, which might be related to the patient characteristics and the lack of PBT standard guidelines.

However, comparative studies have shown that patients treated with laparoscopy had less BTF[7-12]. PBT has been shown to increase the risk of postoperative complications rather than laparoscopic surgery. Results of this investigation showed that there is no causal relationship between PBT and poor prognosis after open gastrectomy. Previous reports showed that the

TABLE 5: UNIVARIATE ANALYSIS OF 5-YEAR DFS

Variable	5-y DFS (%)	P value
Age (y)		0.138
<65	54	
≥65	42	
Sex		0.096
Male	52	
Female	35	
ASA scores		0.189
I-II	49	
III	39	
Number of complications		0.026
No	68	
Yes	42	
Type of gastrectomy		0.242
Total gastrectomy	56	
Distal gastrectomy	41	
TNM staging		0.000
I-II	71	
III	36	
Histodifferentiation		0.158
Differentiation	54	
Undifferentiation	39	
Serious complications		0.071
Yes	59	
No	44	
PBT		0.004
Yes	55	
No	38	

TABLE 6: COX PROPORTIONAL RISK MODEL FOR DFS

Variable	Risk coefficient R	P value
TNM staging (I-II VS III)	1.805 (1.520-2.310)	0.006
Number of complications (<2 VS ≥2)	2.059 (1.269-3.350)	0.010

poor prognosis of patients with GC after PBT is related to the conditions of BTF, but not to the transfusion itself[19-21].

Compared to open gastrectomy, laparoscopic gastrectomy has lower postoperative morbidity, mortality and a similar survival rate in the treatment of GC[7-9]. However, recent evidence suggested that the transformation of patients with GC has a negative effect on long-term exposure. Interestingly, more patients who received BTF eventually chose open gastrectomy in this study. Compared to transition patients who did not receive open surgery, patients treated with open surgery had poorer baseline characteristics.

Previous studies have explained that the lower survival rate of patients with GC after PBT could be due to the underlying cardiovascular or pulmonary disease, which led to a lower threshold for BTF. In addition, the increase of blood cell count during operation is related to the increase of postoperative mortality. These studies suggested that PBT could improve poor prognosis with or without causality.

It was observed that there was no causal relationship between BTF and prognosis in patients treated with laparoscopic gastrectomy in this study. Similar to the results reported of open surgery, here again it was found that poor health status of BTF patients could be associated with poor prognosis[4-6]. Some studies suggested that by reducing BTF and improving surgery, the prognosis can be improved. The advantages of laparoscopic gastrectomy might be related to the need for BTF, which is to protect immune function and reduce intraoperative blood loss. In summary, PBT is associated with decreased OS and DFS in patients treated with laparoscopic radical gastrectomy. This association reflects the clinical condition of patients who needed surgery, but not causality.

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Conflict of interest:

All authors report no conflicts of interest in this work.

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