RESEARCH ARTICLE

Effects of Allogeneic Blood Transfusion in Patients with Stage II Colon Cancer

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Abstract

The aim of the present study was to determine whether allogeneic red blood cell transfusions showed a deleterious effect and what might be preoperative risk factors for blood transfusion in patients with TNM stage II colon cancer. Total 470 patients who fulfilled inclusion criteria were selected for a further 10-year follow-up study. We found that there were statistical significance between non-transfused and transfused group in mortality (*P*=0.018), local recurrence (*P*=0.000) and distant metastasis (*P*=0.040). Local recurrence and distant metastasis between 1 to 3 units and more than 3 units group did not show any significant differences. There was no difference in survival rate between non-transfused and 1 to 3 units group (log rank =0.031, *P*=0.860). The difference between different blood transfusion volume in transfused patients was found (78.77% vs 63.83%, *P*=0.006). Meanwhile, the significant difference of survival rate was existed between non-transfused group and more than 3 units group (84.83% vs 63.83%, *P*=0.002). Univariate analysis showed the following 3 variables to be associated with an increased risk of allogeneic blood transfusions: preoperative CEA level (*P*<0.05), location of tumor (*P*<0.01) and diameter of tumor (*P*<0.01). Multivariate analysis revealed that location of tumor and diameter of tumor are two independent factors for requirement of perioperative transfusions. Therefore, allogeneic transfusion increase the postoperative tumor mortality, local recurrence and distant metastasis in patients with stage II colon cancer. The postoperative tumor mortality, local recurrence and distant metastasis were not associated with the blood transfusion volume. The blood transfusion volume was associated with the survival rate. Location of tumor and diameter of tumor were the independent preoperative risk factors for blood transfusion.

Keywords: Colon cancer - blood transfusion - local recurrence - distant metastasis

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Introduction

Perioperative allogeneic red blood cell transfusion (ABT) is frequently administered for patients undergoing colorectal resection for cancer. Allogeneic blood transfusion was one of the factors on prognosis of colorectal cancer (CRC) in many possible factors (van der Voort van Zijp et al., 2008). It has been reported that allogeneic blood transfusion may potentially increase postoperative tumor recurrence and mortality (Chung et al., 1993; Vamvakas, 1995; Amato et al., 2006). Conversely, other reports have failed to confirm a significant transfusion dependent effect (Weiden et al., 1987; Voogt et al., 1987; Busch et al., 1994). The effect of allogeneic blood transfusion is difficult to describe, because the previous studies all have included all cases without considering the effect of allogeneic blood transfusion might be influenced by different TNM stage. In some studies, CRC stage was considered as an important factors for recurrence (Compton et al., 2000; Kobayashi et al., 2007; Aghili et al., 2010).

Our current study focuses solely on patients with stage II colon cancer and as such avoided the potential confounding factors in other studies, particularly those that have also included rectal cancer.

Materials and Methods

Patients

From 1995 to 2002, there were 1050 patients with colonic cancer who underwent radical operations at fourth affiliated hospital of the China Medical University and Liaoning province tumor hospital. 470 patients who fulfilled inclusion criteria were selected for further following-up study. Inclusion criteria were patients with

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Table 1. Comparison of Patients with Mortality, Local Recurrence, Distant Metastasis and Postoperative Complication in Non-transfused and Transfused Group

Item	Non-transfused Patients(n=211)	Transfused Patients(n=259)	X^2	*P* value
Mortality	32(15.17%)	62(23.94%)	5.592	0.018
Local recurrence	36(17.06%)	86(33.20%)	15.766	0.000
Distant metastasis	18(3.79%)	46(17.76%)	8.421	0.040
Postoperative complication	5(2.37%)	13(5.02%)	2.216	0.137

Table 2. Comparison of Patients with Mortality, Local Recurrence, Distant Metastasis and Postoperative Complication in 1to 3 Units and More Than 3 Units Group

Item	≤3 units Patients (n=212)	>3 units Patients (n=47)	X^2	*P* value
Mortality	45(21.23%)	17(36.17%)	47.18	0.030
Local recurrence	71(33.49%)	15(31.91%)	0.043	0.836
Distant metastasis	38(17.92%)	8(17.02%)	0.021	0.883
Postoperative complication	10(4.72%)	3(6.38%)	0.224	0.636

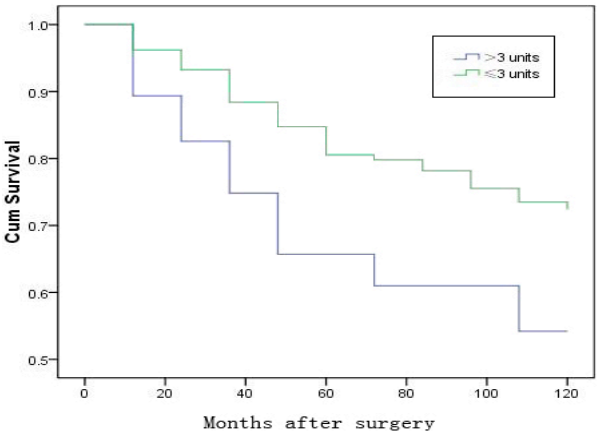

Figure 1. The Survival Curve of the Patients in 1 to 3 Units and More Than 3 Units Group (78.77% vs 63.83%, *P*=0.006)

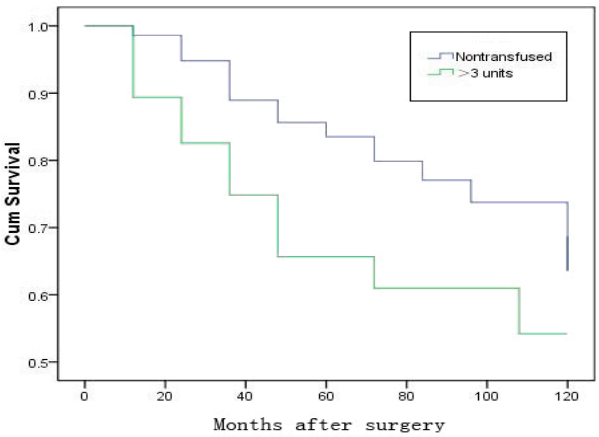

Figure 2. The Survival Curve of the Patients in Non-transfused and More Than 3 Units Group (84.83% vs 63.83%, *P*=0.002)

stage II colon cancer and curative resection. Exclusion criteria were patients who had had chemotherapy or radiotherapy before the operation, had history of blood transfusion or fulfilled Lynch Syndrome. The technique of surgical resection was constant because the operations were only performed by senior surgeons.

The criteria of pathologic classification were according to the World Health Organization (WHO) and UICC/ AJCC.

The criteria of blood transfusion were hemoglobin concentration < 8 g/dl and intaoperative hemodynamic status.

A standard follow-up program was carried out . Physical exammation, chest X-ray, transabdominal ultrasound, laboratory tests and colonoscopy are adopted for follow-up. The last evaluation of follow-up data took place in August 2012.

Statistical analysis

All data were analyzed using SPSS 16.0 for Windows software. The univariate analysis for frequency data including X^2 test or Fisher's exact test were used. A multivariate stepwise logistic regression analysis was performed to identify independent factors in predicting blood transfusion. Differences in survival rate among each group were tested by log rank test. Statistical significance was taken as $P<0.05$.

Results

In the 470 cases, 210 patients were male patients (44.68%) and 260 patients were female patients (55.32%). Mean age was 56.84 (range, 22-81) years. 10-year mortality rate was 20% (n=94), local recurrence rate was 25.96%t (n=122), distant metastasis rate was 13.62% (n=64) and postoperative complication rate was 3.83% (n=18). Patients was 55.11% (n=259) who received perioperative allogeneic red blood cell transfusions. There were 212 patients who received 1 to 3 units and 47 patients who received more than 3 units.

The significant differences of clinical outcomes are existed in the non-transfused and transfused group. Mortality, local recurrence and distant metastasis are more frequently seen in the transfused group (Table 1). Local recurrence and distant metastasis in the blood transfusion volume do not show any significant differences (Table 2).

There is no difference in survival between non-transfused and 1 to 3 units group (log rank =0.031, P=0.860). The difference is found in the group of transfused patients with blood transfusion volume (78.77% vs 63.83%, P=0.006) (Figure 1). Meanwhile, the largest difference was existed between non-transfused group and more than 3 units group (84.83% vs 63.83% , P=0.002) (Figure 2).

Univariate analysis of predictive factors for allogeneic blood transfusion has shown that 3 variables are associated with an increased risk of allogeneic blood transfusions (Table 3): preoperative CEA level ($P<0.05$), location of tumor($P<0.01$) and diameter of tumor ($P<0.01$). Multivariate analysis revealed that only location of tumor and diameter of tumor are independent associated factors for requirement of preoperative transfusions (Table.3).

Table 3. Univariate Analysis and Multivariate Analysis of Predictive Factors for Allogeneic Blood Transfusion

Item	Univariate Analysis			Multivariate Analysis	
	Nontransfused Patients(n=211)	Transfused Patients(n=259)	*P* value	95% CI	*P* value
Age(y)					
≤65	158	184	0.352		*P*>0.05
>65	53	75			
Sex					
Male	89	121	0.325		*P*>0.05
Female	122	138			
Blood type					
A	66	75	0.187		
B	80	80			*P*>0.05
O	50	82			
AB	15	22			
Preoperative CEA level (ng/ml)					
≤5	148	159	0.047		*P*>0.05
>5	63	100			
Location of Tumor(cm)					
Right colon	113	205	0.000	0.225-0.514	0.000
Left colon	98	54			
Gross type					
Protruded type	44	59	0.862		*P*>0.05
Local ulcer type	145	170			
Invasie ulcer type	20	28			
Diffuse ulcer	2	2			
Diameter of tumor(cm)					
<6	104	83	0.000	1.156-2.538	0.007
≥6	107	176			
Tumor stage					
T3	10	18	0.340		*P*>0.05
T4	201	241			
Tumor type					
Mucinous	31	38	0.995		*P*>0.05
Nonmucinous	180	221			

Discussion

Colorectal cancer is one of the most common cancers worldwide with an incidence that continues to increase in many countries (Center et al., 2009). Within the last 3 decades, an extensive amount of results have been reported in order to clarify the effect of allogeneic red blood cell transfusions (ABT) on survival of patients suffering from colorectal cancer. The first report was introduced by Gantt in 1981, who carried out the detrimental effects on cancer patients with blood transfusion (Gantt, 1981). Later some studies have also shown an deleterious effect of ABT (Chung et al., 1993; Vamvakas, 1995; Amato et al., 2006), whereas others did not (Weiden et al., 1987; Voogt et al., 1987 ; Busch et al., 1994). The conclusions of the clinical outcomes are contradictory. Therefore, the question whether blood transfusion is harmful or beneficial to the patients suffering from colorectal cancer can not be answered easily.

The effect of ABT may depend on preoperative stress and host immune system. As an untoward effects, immunosuppression has been speculated to result in decreased tumor surveillance and adverse effects. ABT induced a higher impairment of postoperarive immunity (decreased CD4/CD8 ratio) than a proinflammatory response (high serum levels of IL-6 and IL-10) (Ydy et al., 2007). The immuno -suppressant effect has been related to the blood transfusion volume (Bordin et al., 1999 ; Ikuta et al., 2003 ; Ydy et al., 2007).

To our knowledge, few studies focus on the effect of allogeneic blood transfusion on patients in Dukes B stage of colonic cancer. It is crucial to control the confounding factors to affect the prognosis. In our current study, it has shown that blood transfusion may influence the outcome of mortality, local recurrence and distant metastasis. It was of interest that this kind of difference did not revealed in 1 to 3 units and more than 3 units group, which suggested that the clinical prognosis of patients was not associated with the blood transfusion volume. A similar result was also confirmed in the study of Darko Zdravkovic (Zdravkovic et al., 2011). Therefore, it is important for clinicians to perform extensive follow-up for patients with ABT.

Non-transfused patients has a better survival rate than patients who transfused 1 to 3 units (84.83% VS 78.77%). However, this difference failed to reach statistical significance (P=0.860). The present study demonstrated a dose dependent relationship between blood transfusion volume and survival rate, the more blood transfusion the worse survival rate. It may due to the immunosuppressant effect.

Knowledge of the preoperative risk factors for blood transfusion may be helpful in reducing the use of blood transfusion and improving the survival rate of patients. In our present study, three risk factors associated with the blood transfusion and two were independent risk factors. Location of tumor and diameter of tumor are the most important factors, influencing the blood transfusion. It is commonly known that right colonic cancer is easy to cause anaemic, requiring blood transfusion. With the increased diameter of tumor and level of CEA, an advanced cancer stage might indirectly result in lower initial blood counts and hemoglobin concentration (at the same level of blood loss patients become anaemic), the operation lasted longer and blood loss greater during surgery.

Allogeneic transfusion increase the postoperative tumor mortality, local recurrence and distant metastasis in patients with stage II colon cancer. The postoperative tumor mortality, local recurrence and distant metastasis were not associated with the blood transfusion volume. The blood transfusion volume was associated with the survival rate. Location of tumor and diameter of tumor were the independent preoperative risk factors for blood transfusion

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