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Impact of fresh frozen plasma transfusion on postoperative inflammation and prognosis of colorectal liver metastases



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ABSTRACT

Background: Blood transfusion has been reported to be associated with immunomodulation and poor oncologic outcomes in several malignancies. The aim of the study is to investigate the influence of the use of fresh frozen plasma (FFP) on long-term outcomes in patients with colorectal liver metastases (CRLM) after hepatic resection.

Materials and methods: The study comprised 127 patients who had undergone first hepatic resection for CRLM between April 2000 and December 2013. We retrospectively investigated the influence of the use of FFP on disease-free survival as well as overall survival and assessed the impact of such a practice on postoperative inflammation markers.

Results: In multivariate analysis, more than four lymph node metastases of the primary cancer ($P = 0.001$), bilobar distribution ($P = 0.002$), and perioperative FFP transfusion ($P = 0.005$) were independent risk factors for cancer recurrence, while more than four lymph node metastases of the primary cancer ($P < 0.001$), presence of neoadjuvant chemotherapy ($P = 0.002$), and perioperative FFP transfusion ($P = 0.004$) were independent risk factors for poor overall survival. In patients who underwent FFP transfusion, tumor size ($P = 0.004$), anatomic resection ($P < 0.001$), duration of operation ($P = 0.039$), and intraoperative blood loss ($P < 0.001$) were significantly greater. Moreover, FFP transfusion was associated with a higher white blood cell level on postoperative day 3 ($P < 0.001$) and day 5 ($P = 0.010$) and lower serum C-reactive protein level on postoperative day 1 ($P < 0.001$) and day 3 ($P = 0.017$).

Conclusions: Perioperative FFP transfusion is independently associated with poor long-term outcomes in patients with CRLM after hepatic resection. FFP may have an influence on postoperative inflammation because of its immunosuppressive effects.

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Introduction

The liver is the organ to which colorectal cancer most frequently metastasizes, with 15%-25% of patients having synchronous colorectal liver metastases (CRLM) at presentation and further 25%-50% ultimately developing CRLM after resection of the primary tumor.¹ Hepatic resection is the most effective and potentially curative therapy for CRLM.²⁻⁴ In both surgical and oncologic perioperative managements, significant advances have been made for the treatment of CRLM. However, intraoperative blood loss remains a significant concern in hepatic resection, which is associated with a rather high incidence of blood transfusions including red blood cell concentrate (RBC), fresh frozen plasma (FFP), platelet concentrate (PC), and albumin products.

Recent studies have reported that allogenic blood transfusion exerts immunomodulatory effects,⁵⁻⁷ and blood transfusion may be associated with postoperative complications, earlier disease recurrence, and prognoses of malignancies.⁸ Our previous study reported that FFP transfusion had a negative impact on the overall survival in patients with CRLM.⁹ However, the relationship between FFP transfusion and cancer recurrence or the influence of FFP transfusion on postoperative inflammation is unclear.

Therefore, in this study, we retrospectively investigated the relationship between perioperative FFP transfusion and disease-free as well as overall survival in patients with CRLM after hepatic resection, and we assessed the immunological effect on postoperative inflammatory response.

Patients and methods

Patient selection

Between January 2000 and December 2013, 133 patients with CRLM underwent first hepatic resection at the Department of Surgery, Jikei University Hospital, Tokyo, Japan. Of them, six patients were excluded, two patients for the lack of data and four patients who were lost to follow-up, leaving the remaining 127 patients for this study. We performed a retrospective review of a prospectively maintained database of patients. This retrospective study was approved by the Ethics Committee of Jikei University School of Medicine (#21-121).

Treatment and patient follow-up

All patients underwent macroscopic curative resection for liver, lung, and lymph node metastases. Preoperative chemotherapy was given when liver metastases were unresectable or borderline resectable and discontinued for more than 6 wk before hepatic resection to reduce liver injury and bone marrow suppression by chemotherapy. The extent of hepatic resection was generally determined based on retention rate of indocyanine green at 15 min before surgery and hepatic reserve, as described by Miyagawa et al.,¹⁰ and percutaneous transhepatic portal embolization was performed for patients with estimated residual hepatic volume of less than 30%. The type of resection was classified into two

groups: anatomic resection (extended lobectomy, lobectomy, segmentectomy, or subsegmentectomy) and nonanatomic limited partial resection.

Recurrence of colorectal cancer was defined as newly detected local, hepatic, lung, or extrahepatic tumors by ultrasonography, computed tomography, or magnetic resonance imaging with or without an increase in serum carcinoembryonic antigen (CEA) or carbohydrate antigen 19-9. For recurrent liver metastasis, repeated hepatic resection, local ablation therapy, or systemic chemotherapy was performed based mainly on number, size, and location of the recurrent liver tumors as well as hepatic functional reserve including the retention rate of indocyanine green at 15 min and remnant liver volume. For lung metastasis, limited partial lung resection or systemic chemotherapy was performed. For local recurrence, tumor resection, radiotherapy, or systemic chemotherapy was selected. As to chemotherapy, 5-fluorouracil (5-Fu)-based regimen was chosen as adjuvant and/or neoadjuvant chemotherapy before 2003. Since 2004, the patients received infusional 5-Fu/l-leucovorin with oxaliplatin and/or infusional 5-Fu/l-leucovorin with irinotecan. Since 2007, patients have received 5-Fu/l-leucovorin with oxaliplatin and/or 5-Fu/l-leucovorin with irinotecan with molecular targeting drugs.

Blood products use

Hemogram, chemistry profile, and blood coagulation were routinely measured for each patient preoperatively and on

Table 1 – Patient characteristics.

Factor	Mean ± SD or ratio	Range
Age (y)	64.9 ± 10.2	39-90
Gender (male:female)	91:36	
Primary site (colon:rectum)	79:48	
No. of lymph node metastases (<4:≥4)	102:25	
Timing of tumor (synchronous:metachronous)	67:60	
Neoadjuvant chemotherapy (yes:no)	27:100	
Tumor number (solitary:multiple)	64:63	
Tumor distribution (unilobar:bilobar)	93:34	
Tumor size (mm)	40.8 ± 30.0	4-200
Serum CEA (ng/mL)	180.2 ± 435.3	1.9-2428
Type of resection (anatomic:nonanatomic)	66:61	
Duration of operation (min)	353.9 ± 144.7	85-867
Intraoperative blood loss (g)	1147.7 ± 1890.5	0-19,155
RBC transfusion (yes:no)	43:84	
FFP transfusion (yes:no)	30:97	
PC transfusion (yes:no)	5:122	
Postoperative complications (yes:no)	39:88	

SD = standard deviation; No. = number.

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