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Impact of perioperative blood transfusion on immune function and prognosis in colorectal cancer patients

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ABSTRACT

Objective: To investigate the impacts of perioperative blood transfusion on the immune function and prognosis in colorectal cancer (CC) patients.
Methods: A retrospective analysis was conducted in 1404 CC patients, including 1223 sporadic colorectal cancer (SCC) patients and 181 hereditary colorectal cancer (HCC) patients. Among them, 701 SCC and 102 HCC patients received perioperative blood transfusion. The amount of T lymphocyte subsets and natural killer (NK) cells was measured. All patients received a 10-year follow-up and relapse, metastasis and curative conditions were recorded.
Results: In SCC group, mortality, local recurrence and distant metastasis rate of transfused patients were significantly higher than non-transfused patients (all $P < 0.05$). In HCC group, mortality was apparently higher in transfused patients than non-transfused patients ($P = 0.002$). SCC patients transfused with ≥3 U of blood had significantly higher mortality than patients transfused with <3 U ($P = 0.006$). The amount of T lymphocyte subsets and NK cells showed statistical differences before and after perioperative blood transfusion in SCC and HCC patients (all $P < 0.05$). Also, there existed statistical differences in CD4+/CD8+ ratio among SCC patients before and after the perioperative blood transfusion ($P < 0.05$). CC patients who received perioperative blood transfusion had markedly lower 10-year survival rates as compared with those who did not receive (both $P < 0.05$). SCC patients transfused with ≥3 U of blood had remarkably lower survival rates compared with SCC patients transfused with <3 U ($P = 0.002$).
Conclusions: Perioperative blood transfusion could impact immune function, increased postoperative mortality, local recurrence rate and distant metastasis rate in CC patients; and survival rate of CC patients is negatively related to blood transfusion volume.

1. Introduction

Colorectal cancer (CC) is the third most common type of cancer worldwide making up about 10% of all cases and it is considered among the big killers [1]. In 2012, there were 1.4 million new cases of CC diagnosed and 694,000 deaths from CC [2]. In the western world, 8% of CC is diagnosed as sporadic colorectal cancer (SCC) and approximately 30% of all CC cases belong to the inherited form of the disease [3–5]. Signs and symptoms of CC include blood in the stool, a change in bowel movements, weight loss, and feeling tired all the time [6]. The risk factors for CC include lifestyle, older age, and inherited genetic disorders [7]. Laparoscopic surgery has been a standard treatment of CC for more than 20 years and minimizes access trauma, reduces pain, and accelerates recovery of postoperative bowel functions and is associated with favorable oncological results [8]. However,

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anemia of multifactorial origin at presentation and during the course of the disease is frequent in patients with CC, which may be related to a combination of factors such as iron-deficiency due to occult or overt gastrointestinal blood loss, systemic inflammation with increased hepcidin levels, or secondary to chemotherapy regimens [9]. Therefore, prior to surgery, many patients have a weakened physical condition, and the added blood loss during surgery necessitates perioperative blood transfusion for some patients to insure surgery success [10].

Perioperative allogeneic red blood cell transfusion, as a necessary and life-saving intervention to improve oxygen-carrying capacity and increase peri- and postoperative morbidity and mortality, is reportedly administered in up to 85% patients with CC [1,11]. Thus, despite improvements in surgical techniques, perioperative blood transfusions are routinely needed [12]. The immunomodulation qualities of allogeneic blood transfusion have been appreciated and exploited to prevent renal allograft rejection [13]. The risks of receiving allogeneic blood transfusion have been mitigated by aggressive screening programs, thus the risks of transmission of HIV, and hepatitis C are considered minimal [14]. However, immune modulation by perioperative allogenic blood transfusion might increase susceptibility to infections, cancer recurrence and post-injury multiple organ failure [15]. Some immunological alterations can be seen after blood transfusion including decreased hematopoiesis and interleukin-2 production, impaired natural killer (NK) cell function, reduced T-helper-cell activity, and increased T-suppressor-cell activity [16]. Perioperative blood transfusion is linked with a poor prognosis in lung cancer patients undergoing surgery [12]. In addition, a prior study also revealed that perioperative blood transfusions could promote pancreatic cancer progression and correlate with the poor prognosis in these patients [11].

In our study, we investigated the impact of perioperative blood transfusion on the immune function and prognosis in hereditary colorectal cancer (HCC) and SCC patients. By comparing the amount of T lymphocyte subsets including CD3+, CD4+, and CD8+ cells as well as CD56+ NK cells, CD4+/CD8+ ratio, and the 10-year follow-up clinical data, we hoped to understand the risks of perioperative blood transfusion, and also provide a valuable clinical reference for perioperative blood transfusion in CC patients.

2. Materials and methods

2.1. Ethical statement

This study was approved by the Ethical Committee of the Xiangyang Central Hospital, Heibei. All study participants provided written informed consent.

2.2. Patients

Between January, 1992 and January, 2004, 1404 CC patients receiving radical surgery in the Xiangyang Central Hospital were included according to the following inclusion criteria: (1) patients diagnosed with stage I–III CC and undergoing open radical surgery; (2) patients with absent preoperative radiotherapy and chemotherapy; (3) patients without history of infection within 3 months before surgery; (4) patients without history of other tumors; (5) patients with complete and accurate clinical and pathological data; and (6) patients received follow-up with clear start date, ending date and terminal state. CC was staged based on the 7th edition of the AJCC Cancer Staging Manual for CC [17]. The exclusion criteria were the following: (1) patients with history of blood transfusion, (2) patients with coexistence of other malignant diseases, and (3) patients with distant metastases before radical surgery. Patients (n = 181), who had more than one first-degree relatives diagnosed with CC, were regarded as the HCC group. The remaining 1223 CC patients who did not meet the diagnostic criteria of HCC were regarded as the SCC group. All surgeries were performed by experienced surgeons.

2.3. Perioperative blood transfusion

Criteria of perioperative allogeneic red blood cell transfusion were: (1) hemoglobin (HGB) <6 g/dL, especially during acute hemorrhage; (2) patients with refractory anemia symptoms preoperatively; (3) patients who do not respond to chalybeate, folic acid or vitamin B12 treatment, (4) patients with HGB between 6 and 10 g/dL accompanied by abnormal cardiopulmonary function, increased metabolic rate or progressive blooding. Among the 1223 SCC patients, 701 patients received perioperative blood transfusion, including 362 males and 339 females with average age of 58.06 ± 12.23 years; 522 SCC patients did not receive blood transfusion, including 281 males and 241 females with average age of 58.15 ± 12.38 years. Among the 181 HCC patients, perioperative blood transfusion was performed in 102 patients (46 males and 56 females; average age, 51.83 ± 12.41 years), and not performed in 79 patients (47 males and 32 females; average age, 53.16 ± 11.35 years).

2.4. Measurements of T lymphocyte subsets and CD56+ NK cells

Peripheral venous blood (2 mL) was collected before blood transfusion and 2 days after perioperative blood transfusion, respectively. The collected blood was ethylenediaminetetraacetic acid (EDTA)-anticoagulated, and then the amount of T lymphocyte subsets including CD3+, CD4+, and CD8+ cells, and CD56+ NK cells was measured. The CD4+/CD8+ ratio was calculated.

2.5. Following-up

All patients received a 10-year follow-up to investigate the long-term effects of perioperative blood transfusion. During the follow-up, physical examination and detection of carcinoembryonic antigen (CEA) in blood were carried out every 3–6 months; chest X-ray or computer-aided tomography, abdominal computed tomography (CT) and colonoscopy were performed every 1–3 years. Relapse, metastasis and curative conditions of all patients were recorded. The ending date of the follow-up was September 2014.