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Controversial Role of Blood Transfusion on Outcomes of Patients with Cancer: A Focused Review

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Abstract: Cancer causes a great number of death every year in the world and has been destroying numerous happy families. Both the government and individuals spend vast sums of money on cancer, which makes cancer a great burden to the society. Due to its properties and therapeutic operations, patients with cancer are often accompany with anemia. Red blood cell (RBC) transfusion is a preferred symptomatic treatment strategy. But, considering side effects, optimal protocol of blood transfusion for cancer patients is still in air. Though much work has been done, there are still continuous arguments on the adverse effects of blood transfusion on cancer prognosis. By reviewing these works, we focused on the essential elements of transfusion, i.e. the time and dose of blood transfusion, as well as the type and source of blood product. Though we failed to find a definite answer, previous studies indicated some clues on the relationships between cancer prognosis and these elements. Transfusion prior to surgery and reduction of intraoperative and postoperative blood demand may be beneficial. As for RBC type, autologous leucocyte-depleted RBC might have priority. However, more high-quality randomized clinical trials are needed to settle those questions. Furtherly, this narrative review suggested some critical ideas on further studies.

Keywords: Blood Transfusion, Cancer, Prognosis

1. Introduction

Cancer is a leading cause of death in China as well as worldwide. According to National Central Cancer Registry of China, incidence rate of cancer in China was 278.07/100,000 in 2014, much higher than that of the world average [1]. Until 2017, with about 62.9 million disability-adjusted life years, the cancer burden of China is still heavy [2]. It is reported that approximately 50% of cancer survivors underwent cancer-related financial distress [3]. Though a vast proportion of resources have been devoted to improve prognosis of cancer, many iatrogenic factors impact therapeutic effect, blood transfusion included [4].

Blood transfusion is an efficient way to treat anemia. As a deeline, patients with cancer often exist the anemic phenomena of different extent. Perioperative blood loss aggravates the situation. Thus, blood transfusion is not rare among cancer patients. It is reported that perioperative blood use is connected with impairment of immunologic function [5, 6]. Some studies have reported that there were associations between blood transfusion and the prognosis of these patients [7-9]. However, some studies showed different results [10-12]. We hypothesized that the time and dose of blood transfusion, as well as the type and source of blood product might account for these diverse results. Therefore, we made this systematic review to explore the association between blood transfusion and outcomes of cancer patients.

2. Connections Between the Time of Blood Transfusion and Prognosis of Cancer

One of the most important roles of blood transfusion is to increase the concentration of hemoglobin (Hb). In clinical practice, transfusion indication has not reached a consensus due to complicated situations. We found that the standard of

blood transfusion for cancer patients was not well established. In a retrospective study, the preoperative Hb level of transfused group was 8.5 (4.7-13.1) g/dL, while non-transfused group was 12.2 (5.7-16.0) g/dL [13]. One conclusion of this study was perioperative blood use shortened overall survival (OS) of colorectal cancer patients. A cohort study, suggesting worse outcomes of colorectal cancer patients in transfused group, showed that patients who received blood had a lower preoperative Hb (106 (98–121) g/L vs. 133 (124–146) g/L) [14]. According to a JAMA article focusing on recommendations of patient blood management, when hemoglobin concentration is less than 7.0g/dL, red blood cell (RBC) should be transfused before major surgery [15]. Nevertheless, clinical blood use is relatively less rigid. Considering the connections between blood transfusion and outcomes of cancer, blood use should be more circumspect. Thus, the time of perioperative transfusion (i.e. the threshold of Hb) still needs more evidence-based recommendations.

Blood transfusion could be conducted preoperatively, intraoperatively and postoperatively. A retrospective study enrolled 117 colorectal cancer patients clued that preoperative transfusion aiming to correct anemia did not significantly impact survival [16]. On the contrary, Marco et al [17] proposed that there was association between transfusion and OS and cancer-specific survival (CSS) in nonanemic population. They further demonstrated that intraoperative transfusion suggested poor outcomes of bladder cancer sufferer [18]. Buchner et al [19] made a parallel retrospective analysis and they found that intraoperative or postoperative blood use had a significant detrimental impact on OS and CSS. In this regard, correction of anemia prior to surgery and measures of reducing intraoperative and postoperative blood demand lay great importance to patients with cancer.

3. The Dose of Blood Transfusion

The volume of transfused blood is dependent mainly on the anemia degree and intraoperative blood loss. Studies have demonstrated transfusion deteriorated outcomes of cancer in a dose-dependent manner. Li et al [5] found that if the amount of blood was more than 3 units, patients underwent colorectal cancer surgery had a remarkably higher mortality. Buchner et al [19] reached a similar conclusion that bladder cancer patients without RBC transfusion had a relatively longer CSS, 1-2 units of RBC reduced CSS, while RBC units.>2 represented a worst CSS. A recent study by Latif et al [20] seems to be more interesting. In their work, no significant differences had been observed between 0 and 1 unit RBC, while with the transfusion volume increasing to 2, 3-7 and >=8 units, OS and disease-free survival (DFS) decreased, but cumulative incidence of recurrence increased. Though specific threshold value of blood that represents a significant worse prognosis has not been defined, the dose-effect relationship is remarkable.

4. The Type of Blood

The purposes of perioperative blood transfusion often include increasing oxygen carrying capacity and improving coagulation function. Some studies have indicated that the type of transfused blood might lead to diverse outcomes. A prospective and randomized clinical trial by Jan et al [21] focusing on the near-term outcomes and long-term survival of colorectal cancer, compared the different effects of packed RBC and leucocyte-depleted RBC. Ventilation support in intensive care unit and hospital stays of leucocyte-depleted RBC group were significantly superior to that of packed RBC group. Though difference of long-term survival of the two groups was not significant, patients with leucocyte-depleted RBC seemed to have a longer survival (55 vs. 36 months). Similar findings were observed in two other studies [22, 23]. An interesting retrospective study reported that transfusion of cytokine-induced killer cells enhanced cancer control and prolonged survival time of advanced pancreatic cancer patients [24]. Unfortunately, the sample is relatively small and more prospective studies are needed.

5. Autologous or Allogeneic Blood

Autologous blood transfusion is widely recognized as a safe therapeutic strategy. Compared with allogeneic blood, autologous blood had little impact on immune function and largely reduced the risk transfusion-related infection. Therefore, some studies have attached attention to the influences of autologous and allogeneic blood on cancer prognosis. A small sample study, analyzed survival of esophageal cancer patients, showed an evident advantage of autologous transfusion over allogeneic transfusion [25]. The clinicians further drew a same conclusion within recurrent esophageal cancer patients [26]. Kim et al [27] did a 2713-person retrospective study in which the roles of perioperative blood transfusion, autologous transfusion and allogeneic transfusion on CSS, OS and biochemical recurrence-free survival (BRFS) of prostate cancer were determined. In virtue of the Kaplan-Meier survival analysis, allogeneic transfusion was considered as a predictor of poor CSS, OS and BRFS, while differences between autologous transfusion and non-transfusion did not reach significance. However, a study on non-small cell lung cancer had a different conclusion. In this study, multivariate Cox regression analysis indicated that the source of blood (autolpgous or allogeneic) was not an independent factor for survival [28]. This disagreement might be explained by the previously discussed issues. But more importantly, we recommend autologous blood transfusion unless there is more high-level evidence. Considering the difficulties of autologous blood preparation and storage, as well as the possibility of intraoperative blood demand, it is of great necessity to investigate the role of autolpgous or allogeneic transfusion on outcomes of cancer.

6. Conclusion

Blood transfusion is an effective way to improve anemia for patients with cancer. The mentioned four factors do have influences on outcomes of cancer patients. But, some effects are still controversial. According to the current studies, we recommend autologous leucocyte-depleted RBC transfusion prior to surgery and reduction of intraoperative and postoperative blood demand. Thus, clinical doctors should make efforts to minimize blood use and make an optimized transfusion plan. More importantly, convincing clinical trails are on urgent.

Conflict of Interest Statement

All the authors do not have any possible conflicts of interest.

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