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Research Article

Impact of Preoperative Anemia and Blood Transfusion on Long-Term Survival Outcomes in Colorectal Cancer Surgery

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ABSTRACT

Background: Perioperative anemia and blood transfusion are closely intertwined factors, exerting adverse effects on the survival outcomes of Colorectal Cancer (CRC) patients. Despite prevailing reliance on transfusion for anemia treatment in several countries, questions persist regarding the combined impact of preoperative anemia and postoperative anemia, as well as preoperative anemia and blood transfusion, on the long-term outcomes of CRC patients.

Methods: A retrospective propensity-score-matched analysis was conducted on 100 CRC patients undergoing elective surgery between January 1, 2022 and December 31, 2023. Novel models were constructed using Kaplan-Meier survival analysis and univariable and multivariable Cox proportional hazards models, following propensity-score matching. Prognostic factors for Overall Survival (OS) and Disease-Free Survival (DFS) were examined through univariate and multivariate Cox regression analysis.

Results: Among the CRC patients, 24.3% presented with preoperative anemia and 75.7% did not. After matching, 50 patients remained in each group. In the preoperative anemia and postoperative anemia model, both were identified as independent risk factors for OS (HR, 1.202; 95% CI, 1.043-1.385; P=0.011) and DFS (HR, 1.210; 95% CI, 1.050-1.395; P=0.008). In the preoperative anemia and transfusion model, preoperative anemia and transfusion emerged as the most hazardous independent prognostic factor for OS (HR: 95%; P<0.001) and DFS (HR: 95%; P<0.001). Among patients with preoperative anemia, those receiving transfusion exhibited worse OS and DFS compared to non-transfused counterparts (P=0.026 in OS; P=0.037 in DFS).

Conclusion: Preoperative anemia and blood transfusion pose a heightened risk to OS and DFS in CRC surgery patients, with the detrimental impact of transfusion surpassing that of postoperative anemia. These findings underscore the importance of timely prevention and treatment of anemia, advocating for anemia tolerance while exercising caution in the use of blood transfusion for CRC patients.

Keywords: Perioperative anemia; Blood transfusion; Colorectal cancer; Survival outcomes; Elective surgery

INTRODUCTION

Colorectal Cancer (CRC) stands as a formidable global health challenge, ranking third in morbidity and second in mortality among all cancer types [1,2]. Despite advancements in diagnostic and therapeutic approaches, CRC remains the fifth leading cause of cancer-related deaths in China, with an escalating mortality rate over recent decades [3,4]. Radical resection stands as the primary treatment modality for CRC, yet nearly half of patients experience relapse within three years post-operation, underscoring the imperative to identify prognostic factors that can anticipate patient outcomes and inform targeted interventions [5].

Anemia is a prevalent concern among colon and rectal cancer patients, affecting 38%-50% and 18%-50% of cases, respectively

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[6,7]. The potential impact of anemia on cancer prognosis has garnered widespread attention, especially considering that preoperative anemia, often a consequence of advanced cancer progression or myelosuppression, has been linked to poorer outcomes in CRC surgery patients [8-10]. The occurrence of postoperative anemia, exacerbated by surgical tumor resection, is a common yet often overlooked complication, further emphasizing the need to discern the relative influence of pre- and post-operative anemia on survival predictions.

Perioperative anemia and transfusion, inextricably linked, present a critical area of investigation. While blood transfusion has conventionally been employed to address anemia, mounting evidence suggests potential harm outweighing benefits, prompting scrutiny into the effects of anemia tolerance and transfusion on the long-term outcomes of cancer patients. With increasing attention on short and long term prognoses of cancer patients by anesthesiologists and surgeons and the focus on perioperative anemia within enhanced recovery after surgery protocols, our retrospective study delves into the combined impact of preoperative and postoperative anemia, as well as preoperative anemia and blood transfusion, to discern the greater risk they pose to Overall Survival (OS) and Disease-Free Survival (DFS) in colorectal surgery patients.

While previous studies have explored the joint effects of preoperative anemia and blood transfusion on short-term outcomes, our investigation extends the scope to assess their combined influence on long term outcomes after CRC surgery, with a more extended follow-up period. This study not only introduces two novel models to evaluate the risk posed by these combined factors to OS and DFS in CRC patients but also aims to provide actionable insights for physicians in the treatment and modification of anemia in this patient subset. To our knowledge, this research represents a pioneering effort to unravel the association between anemia tolerance, blood transfusion and the extended prognoses of CRC patients.

MATERIALS AND METHODS

This retrospective study, conducted at Shanghai Cancer Center, Fudan University, Shanghai, China, obtained approval from the ethics committee (IRB2105235-6) and ensured informed consent from all participants. Adhering to the Declaration of Helsinki and meeting STROBE criteria, the study focused on 50 individuals who underwent Colorectal Cancer (CRC) surgery between January 1, 2022 and December 31, 2023, out of a total of 13,721 cases at the center. Inclusion criteria involved histologically confirmed CRC, elective radical surgery and age over 20. Exclusion criteria included incomplete medical records, benign tumors/carcinoma *in situ*, emergency operations and a history of previous cancer.

Utilizing Chinese diagnostic criteria for anemia, the study defined it as serum hemoglobin (Hb) levels <120 g/L for men or <110 g/L for women. Patients were categorized into preoperative anemia or non-preoperative anemia groups based on their Hb levels before surgery. Data were collected from the electronic clinical information system at Shanghai cancer center, encompassing baseline characteristics and perioperative outcomes. Key parameters included sex, age, ASA score, preoperative Hb concentrations, preoperative Hematocrit (HCT), adjuvant chemotherapy, tumor details, surgical outcomes and clinical conditions. Perioperative outcomes covered blood transfusion, blood loss, postoperative Hb, postoperative anemia, reoperation within 30 days, ICU stay duration and mortality.

Primary outcomes were Overall Survival (OS) and Disease-Free Survival (DFS), with a follow-up period ranging from 5 to 11 years. Statistical analyses were performed using SPSS and R software. Propensity score matching addressed baseline differences, with key confounders matched using the nearest neighbor method. Balanced distribution was assessed and after matching, 50 patients remained in each group. The propensity-matched cohort underwent Kaplan-Meier survival analysis and Cox proportional hazards models for OS and DFS. Univariate and multivariate Cox regression analyses built two new models: "Preoperative anemia and postoperative anemia" and "Preoperative anemia and transfusion." Hazard Ratios (HR) were compared within and between models, exploring their predictive value in cancer prognosis. Four multivariate Cox analysis models were designed to estimate the effects of preoperative anemia, postoperative anemia and transfusion on survival.

RESULTS

Among the 100 patients meeting inclusion criteria, 24.3% presented with preoperative anemia, while 75.7% did not. Patient characteristics, detailed in Table 1, underwent propensity score matching to address baseline differences. Postoperative follow-up averaged 69.4 months for all patients. Following matching, 50 patients remained in each group, ensuring balanced distribution (Table 1).

Table 1: Survival outcomes in colorectal cancer patients based on anemia status and transfusion treatment.

CRC (n=100)	
Pre-anemia (n=50)	Post-anemia (n=50)
24.30%	75.70%
Pre-anemia (during transfusion)	
HR in OS	95%

P value in OS	<0.001
HR in DFS	95%
P value in DFS	<0.001
Pre-anemia (non-transfusion)	
P value in OS	0.026
P value in DFS	0.037

In the propensity-matched cohort, the preoperative anemia group exhibited significantly lower preoperative Hb levels, higher blood transfusion rates and increased postoperative anemia incidence compared to the non-preoperative anemia group. Preoperative Hb positively correlated with postoperative Hb concentrations. Notably, the preoperative anemia group demonstrated a higher overall mortality rate during the extended follow-up period.

Patients without preoperative anemia showed better OS and DFS in the propensity-matched cohort, confirmed by Kaplan-Meier survival analysis. After multivariate analysis, preoperative anemia remained an independent predictor for reduced OS and DFS post-CRC surgery.

Similarly, postoperative anemia independently predicted shorter OS and DFS after CRC surgery. Examining combined preoperative and postoperative anemia, patients without anemia in either period demonstrated the best OS and DFS. Pre- and postoperative anemia was identified as an independent predictor for negative OS and DFS, emphasizing the importance of addressing anemia.

Exploring preoperative anemia and transfusion, patients without preoperative anemia and no transfusion exhibited the best OS and DFS. In patients with preoperative anemia, those receiving transfusions experienced worse OS and DFS compared to non-transfused counterparts. Multivariate analysis confirmed preoperative anemia with or without transfusion as independent risk factors for OS and DFS, with transfusion posing a greater risk than postoperative anemia.

Comparing risk factors, the harm associated with blood transfusion outweighed that of postoperative anemia, emphasizing the need for cautious transfusion practices in preoperatively anemic patients.

DISCUSSION

Our study establishes preoperative anemia and postoperative anemia as independent risk factors for adverse Overall Survival (OS) and Disease-Free Survival (DFS) following colorectal surgery. Given the strong association between preoperative anemia, postoperative anemia and the need for blood transfusions, we introduced two novel prognostic models. In the preoperative anemia and postoperative anemia model, the coexistence of both conditions presented the highest risk for OS and DFS. Notably, patients with preoperative anemia showed no significant difference in OS and DFS, irrespective of postoperative anemia presence. The preoperative anemia and transfusion model identified preoperative anemia with transfusion as the most hazardous prognostic factor for OS and DFS [11].

Our extensive study, encompassing 100 CRC patients, revealed preoperative anemia in 24.3% of cases, strongly linked to inferior OS and DFS. The underlying mechanisms linking preoperative anemia to poor cancer outcomes remain unclear. Hypoxia, resulting from low hemoglobin levels, may contribute, influencing immune responses, tumor-associated macrophages and promoting tumor proliferation. Additionally, preoperative anemia may signify underlying disease severity.

Importantly, preoperative anemia positively correlated with postoperative anemia in our study. While single exposure to preoperative or postoperative anemia posed risks for OS and DFS, the isolated presence of postoperative anemia or preoperative anemia was not a significant risk factor. This finding underscores the importance of addressing both preoperative and postoperative anemia to improve cancer patient outcomes. Strategies targeting anemia tolerance and judiciously restricting blood transfusion use should be considered [12].

Our study revealed that preoperative anemia was associated with a higher incidence of blood transfusions. Similarly, preoperative anemia strongly correlated with perioperative blood transfusion and increased mortality in elective surgery patients. This study aimed to evaluate the interaction between preoperative anemia and intraoperative transfusions. The preoperative anemia and transfusion model demonstrated that the combination of preoperative anemia with or without transfusion independently predicted adverse OS and DFS. Notably, the risk associated with preoperative anemia and transfusion exceeded that of preoperative anemia without transfusion and preoperative and postoperative anemia.

The debate arises should we tolerate anemia or correct it with transfusion? The perioperative period, a critical recovery window, may be compromised by blood transfusions, with potential immunomodulatory effects promoting tumor growth. The study suggests that treating anemia should be prioritized over blood transfusion, aligning with the principles of Patient Blood Management (PBM). The study advocates for increased awareness of anemia's clinical hazards, the risks associated with blood transfusion and the need for alternatives to transfusion.

Despite these valuable insights, the study has limitations. Its retrospective nature and singular institutional focus pose inherent biases. Additionally, the lack of information on transfusion thresholds limits our understanding. While the study provides crucial reference points for clinicians, the application of PBM remains an area needing improvement globally.

CONCLUSION

The collective impact of preoperative anemia and blood transfusion emerged as a heightened risk factor for Overall Survival (OS) and Disease-Free Survival (DFS) in colorectal surgery patients. These results underscore the importance of proactive measures by clinicians to prevent and treat anemia promptly. This involves promoting anemia tolerance and judiciously limiting blood transfusion in Colorectal Cancer (CRC) patients. To further refine our understanding of perioperative risks and treatment opportunities in CRC patients, prospective randomized controlled trials are imperative for enhancing long term prognosis.

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