The Effect of Preoperative Anemia on Postoperative Morbidity and Mortality in Patients Undergoing Thoracic Surgery

Torasik Cerrahi Geçiren Hastalarda Preoperatif Aneminin Postoperatif Morbidite ve Mortaliteye Etkisi

Keywords: anemia, morbidity, mortality, thoracic surgery

ABSTRACT

Objective: Anemia is common in patients undergoing thoracic surgery due to three main risk factors including iron deficiency, chronic disease and iatrogenic factors, all of which can be prevented and treated. Our hypothesis was that the incidence of anemia may be higher than expected and associated with perioperative complications.

Method: The data belonging to a total of 107 adult patients were included in the final analysis. We recorded demographic features, pre- and postoperative laboratory findings, comorbidities, blood transfusion rates, complications, mortality, type of surgery, rate of re-exploration, and duration of hospital stay.

Results: The incidence of anemia was 43.9%, being higher in men with 57.4 percent. Anemic patients had a significantly prolonged hospital stay, higher rate of ICU hospitalizations, higher levels of pre- and postoperative creatinine and lower levels of postoperative Hb, Htc and preoperative INR (p<0.05).

Conclusion: Even though the rate of mortality was not affected, anemia was associated with a higher rate of ICU admission and longer hospital stay. In order to reduce anemia-induced perioperative complications, the treatment of preoperative anemia should be considered for thoracic surgery patients.

Received/Geliş: 25.09.2020
Accepted/Kabul: 26.11.2020
Published Online/Online yayınlan: 31.12.2020

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INTRODUCTION

Anemia is the most common hematological problem encountered in the preoperative period prior to a major elective surgery. The incidence of preoperative anemia ranges from 5% to 75% in surgical procedures [1]. There is limited data on the incidence of preoperative anemia in patients undergoing thoracic surgery. Chamogeorgakis et al. [2] analysed the data of 214 early stage non-small cell cancer patients undergoing surgery. They revealed in their study that the incidence of preoperative anemia was 28% in male and 8% in female patients. In another study, anemia was determined in 33% of patients with non-small cell lung cancer [3]. According to European Cancer Anemia survey, the incidence of anemia in patients with lung cancer was 37.6 percent [4].

Although preoperative anemia is a serious problem increasing the risk for preoperative RBC transfusion, morbidity, and mortality, it may not be of primary concerns of surgeons [5]. It has been known since long time that preoperative anemia increases the risk for postoperative complications, extends the length of hospital stay, and is associated with death. Nevertheless, often surgical teams generally do not take preoperative anemia into account as a risk factor and do not take sufficient necessary steps to correct the problem [6]. A study analyzing the risk factors associated with postoperative mortality and morbidity in a patient undergoing lung cancer resection demonstrated that preoperative anemia is closely associated with mortality [7]. Inflammation and anemia are common findings and independent prognostic factors in patients with lung cancer [8]. In a study including a total of 124 patients undergoing surgery for small cell lung cancer, it was reported that preoperative anemia had a significant effect on survival and lung cancer-specific mortality [2].

The hypothesis of this retrospective study is that the incidence of anemia may be higher than expected. Therefore, our primary aim was to analyze the incidence of preoperative anemia along with the associated postoperative complications. The secondary aim was to determine the consequences of anemia in patients undergoing thoracic surgery.

MATERIALS and METHODS

Ethical approval for this study (Ethical Committee No:09.2018.137) was obtained from the Ethical Committee of our University Hospital on 02.02.2018. We retrospectively analyzed the data belonging to a total of 110 adult patients undergoing thoracotomy or thoracoscopy between January, 2016 and July 2017. In case that a patient had multiple surgeries, only the data of the first surgery was taken into consideration. Patients, who had urgent surgery; aged below 18 years; with a known bleeding disorder; and those with renal insufficiency, hepatic insufficiency, or congestive heart failure were excluded from the study.

We recorded demographic features including age, gender, body mass index and ASA scores, preoperative laboratory blood test results including hemoglobin level, INR, creatinine and platelet counts, comorbidities, blood and blood product transfusions, complications, mortality, type of surgery, rate of re-exploration, length of Intensive Care Unit (ICU) and length of hospital stay. Patients were classified into two groups according to the presence or absence of preoperative anemia. The anemia was defined according to the World Health Organization (WHO) criteria as a hemoglobin level <12 g/dL in women and <13,0 g/dL in men [9]. Besides the patients were devided into two groups according to their requirement of treatment in ICUs and hospital wards. The demographics, types and duration of surgery, duration of hospital stay, perioperative laboratory values, the amount of bleeding, the consumption of blood products and complications were compared among ICU and non-ICU patients. The duration of surgery, amount of RBC transfusion, length of hospital stay, preoperative Hb and Htc values were also compared according to univariable and multivariable models using 95% confidence limits.
### Statistical Analysis

The SPSS 22.0 program was used for the analysis of the study data. The descriptive statistics employed in the study were mean, standard deviation, median, minimum, maximum, frequency, and ratio. The Kolmogorov-Smirnov test was used to measure the distribution of variables. The Mann-Whitney U test was used to analyze quantitative independent data while the chi-square test was used to assess the qualitative independent data. In cases where the chi-square test conditions were not met, the Fisher test was used for the qualitative data. A value of \( p < 0.05 \) was considered statistically significant.

### RESULTS

The thoracic operations performed for our patients were decortication, lobectomy, pneumonectomy, and sleeve lobectomy (Table 1). Three patients were excluded from the study because of missing data and ultimately the data on a total of 107 patients were analyzed within the scope of the study. The mean incidence of anemia was 43.9% among women, being higher in men with a rate of 57.4 percent. The groups with and without anemia did not significantly differ by age, gender distribution, BMI, ASA class distribution, the length of surgery, and ICU stay, preoperative platelet transfusion rate, and perioperative platelet transfusion.

#### Table 1. Comparison of patient demographics, type of surgery, the duration of hospital and ICU stay, parameters for perioperative hematologic evaluation, the requirement for blood products and postoperative complications between patients with and without anemia.

|                      | Anemia (-) | Anemia (+) | \( p \) | m  |
|----------------------|------------|------------|--------|----|
| **Age (years)**      | Mean±sd/n (%) | Median     | Mean±sd/n (%) | Median | 0.967 | X²  |
| Gender               |            |            |        |     |
| Female               | 61.37±12.20 | 62.50      | 60.89±13.79 | 62.00 | 0.800 | m   |
| Male                 | 27 (45.0%) | 20 (42.6%) | 27 (57.4%) |       |       |     |
| **BMI**              | 26.19±4.11 | 26.10      | 25.11±5.03 | 25.80 | 0.855 | m   |
| **ASA**              | 2.87±1.14  | 3.00       | 2.91±1.14 | 3.00  | 0.805 | m   |
| **Type of surgery**  |            |            |        |     |
| Decortication        | 7 (11.7%)  | 3 (6.4%)   | 0.591   | X²  |
| Lobectomy            | 46 (76.7%) | 36 (76.6%) |         | m   |
| Pneumonectomy        | 3 (5.0%)   | 5 (10.6%)  |         | m   |
| Sleeve resection     | 4 (6.7%)   | 3 (6.4%)   |         | m   |
| **Duration of surgery (h)** | 4.14±1.43  | 4.07±1.57 | 0.663   | m   |
| **Hospital stay (days)** | 7.98±2.98  | 9.96±5.81 |         | m   |
| **ICU stay (days)**  | 12 (20.0%) | 21 (44.7%) | 0.006   | m   |
| **Preoperative Hb (g/dl)** | 13.74±1.07 | 11.10±1.36 | 0.000   | m   |
| **Postoperative Hb (g/dl)** | 11.29±1.54 | 10.25±1.66 | 0.002   | m   |
| **Preoperative Htc (%)** | 41.32±3.26 | 34.24±4.38 | 0.000   | m   |
| **Postoperative Htc (%)** | 34.98±4.07 | 30.10±4.17 | 0.000   | m   |
| **Preoperative INR**  | 0.98±0.22  | 1.14±0.64 | 0.038   | m   |
| **Postoperative INR** | 1.22±1.30  | 1.16±0.18 | 0.017   | m   |
| **Preoperative Creatinine (mg/dL)** | 0.82±0.18 | 1.36±4.42 | 0.006   | m   |
| **Postoperative Creatinine (mg/dL)** | 0.83±0.29 | 0.70±0.26 |         | m   |
| **Preoperative Platelet (×10⁹/L)** | 279.0±101.7 | 279.9±114.3 | 0.770   | m   |
| **Perioperative bleeding (mL)** | 495±378 | 383±262 | 0.155   | m   |
| **Perioperative fluid (mL)** | 1385±614 | 1306±413 | 0.957   | m   |
| **Perioperative urine output (mL)** | 417.0±231.4 | 405.3±243.1 | 0.788   | m   |

\( m \) Mann-whitney u test / X² chi-square test
fluid administration, perioperative urination and bleeding, and intraoperative Fresh Frozen Plasma (FFP), platelet suspension and RBC transfusion rates. Similarly, no significant difference was observed between the anemic and non-anemic groups regarding the RBC, FFP, platelet transfusion rates, Deep Vein Thrombosis (DVT), and MI as well as the rate of stroke, severe arrhythmia, mortality and re-exploration in the postoperative period (p>0.05, Table 1). Compared with the patients without anemia, the patients with anemia had a significantly increased length of hospital stay, higher rate of ICU admission, higher levels of pre- and post-operative creatinine, lower levels of postoperative Hb and Htc, and lower value of preoperative INR (p<0.05, Table 1).

When the patients admitted to the ICU were compared with those who did not require intensive care, no significant difference was detected between the groups regarding age, gender distribution, ASA class,
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Table 3. The comparison of significant effectiveness in univariable and multivariable models.

|                              | Univariable Model |                          |                          | Multivariable Model |                          |                          |
|------------------------------|-------------------|--------------------------|--------------------------|---------------------|--------------------------|--------------------------|
|                              | OR                | 95% confidence bounds    | p                        | OR                  | 95% confidence bounds    | p                        |
| Duration of surgery (h)      | 1.9               | 1.3-2.7                  | **0.000**                | 2.0                 | 1.4-2.9                  | **0.000**                |
| RBC transfusion (U)          | 4.0               | 1.4-11.4                 | **0.011**                |                     |                          |                          |
| Length of hospital stay (days)| 1.3               | 1.2-1.5                  | **0.000**                |                     |                          |                          |
| Preoperative Hb (mg/dL)      | 0.7               | 0.6-0.9                  | **0.010**                |                     |                          |                          |
| Preoperative Htc (%)         | 0.9               | 0.8-1.0                  | **0.013**                | 0.9                 | 0.8-1.0                  | **0.008**                |

**Logistic Regression**

Preoperative anemia is a common condition in patients undergoing major elective surgery. The most common reason in the etiology of preoperative anemia is iron deficiency [10,11]. Iron deficiency anemia, anemia of chronic disease, and iatrogenic anemia are three most common causes in patients undergoing thoracic surgery [12]. We included the patients who had decortication, lobectomy, pneumonectomy, and sleeve lobectomy in this study. These patients generally had chronic diseases such as cancer in etiology. The major causes of anemia in lung disease-related cancers include impaired intestinal iron absorption and reduced bone marrow response to erythropoietin [13].

Preoperative anemia increases the incidence of mortality in both adult and pediatric patients [14]. One of the main causes of the increase in mortality is the elevation in the frequency of blood and blood product transfusions. Neither the anemic nor the non-anemic groups showed a significant rise in the intraoperative or postoperative levels of RBC, FFP or the use platelets. Furthermore, the incidence of the complications including postoperative MI, arrhythmias, re-exploration or exitus was also similar between the groups. We, however, identified that the most significant adverse result of anemia in patients undergoing thoracic surgery is extended length of hospital and ICU stays. Our study also indicated that the patients admitted to the ICU experienced longer hospital stay, longer operative times and increased use of intraoperative RBC. It may be specula-

In the univariate model, the duration of surgery and hospital stay, the amount of intraoperative RBC transfusion, preoperative Hb and Htc levels had a significant effectiveness (p<0.05). In the multivariate model, the duration of surgery and preoperative Htc values were independent effective factors (p<0.05, Table 3).

**DISCUSSION**

In the present study, preoperative anemia was found to be associated with extended length of stay at hospital and ICU. In the anemic group, the perioperative creatinine level was significantly higher, and the duration of surgery and the total length of hospital stay were longer in the patients admitted to intensive care unit.

type of surgery, body mass index (BMI), postoperative Hb, INR, creatinine, platelet, RBC, preoperative INR, creatinine, platelet values, perioperative fluid level, urination, bleeding, and intraoperative transfusions of FFP, and platelet suspension, postoperative DVT, MI, postoperative stroke, severe arrhythmia, and rates of mortality and re-exploration (p>0.05, Table 2). Patients who required ICU admission significantly differed from those who did not, as for lower levels of preoperative Hb, pre- and postoperative Htc levels and increased duration of operation, hospital stay, and higher intraoperative RBC use (p<0.05, Table 2).
ted whether anemia in the study cohort may represent a marker for more sick patients rather than an isolated reduction in hemoglobin mass.

A study analyzing the data on 189 patients having pulmonary resection demonstrated an increased incidence of respiratory and infectious complications in anemic patients [15]. The Enhanced Recovery After Surgery (ERAS) protocol aiming to identify and eliminate patients’ nutritional deficits in the preoperative period has been put into practice [16]. This protocol enables the optimization of patients before surgery including preoperative treatment of anemia, and thereby, facilitates the operation of patients.

Preoperative and intraoperative anemia has been identified as a risk factor for acute kidney injury (AKI) [17]. In the present study, we followed up the perioperative creatinine clearance and urine output levels. Whereas perioperative urine output did not significantly differ between groups, perioperative creatinine levels were found to be significantly higher in the anemic group. The incidence of AKI has been reported to be high in cardiac surgeries and transplantation procedures [18]. This study proves that preoperative anemia is associated with AKI in thoracic surgeries. This addresses that microcirculation perfusion can not be adequately maintained in anemic patients.

In recent years, there have been studies reporting that blood transfusion increases the chance of recurrence in patients undergoing surgery for lung cancer [19]. In fact, this is a controversial issue as there are also studies arguing that blood transfusion has no effect on recurrence. However, it is unquestionable that patients that have preoperative anemia before pulmonary resection and thus receive blood transfusion develop poor outcomes. The direct growth factor action plays a key role on transfusion-associated immune suppression and lung cancer cells [20].

Limitations
Our study has some limitations due to its retrospective nature. In our analyses, we did not include different types of surgical procedures such as mediastinoscopy, which might influence the study results. The low number of the patients, whose complete medical data we were able to access, was also a limitation.

Conclusion
Consequently, the incidence of preoperative anemia was found to be higher (43.9%) in patients undergoing pulmonary resection. It was determined that even though preoperative anemia did not generally cause a significant increase in the mortality rate or create a risk for perioperative blood transfusion, it extended the length of hospital and ICU stays and it is an important predictor associated with AKI development. In this regard, we believe that the treatment of preoperative anemia should be considered to reduce anemia-induced perioperative complications for thoracic surgery patients.

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