Association between Preoperative Hemoglobin and Postoperative Moderate and Severe Anemia among Patients undergoing Total Knee Arthroplasty

Abstract

Introduction: Anemia is a critical concern in both internal medicine and surgery, with significant effects on overall health and surgical outcomes. The relationship between preoperative hemoglobin levels and moderate to severe postoperative anemia in patients undergoing total knee replacement (TKR) surgery was investigated at a teaching hospital. The goal was to identify factors influencing the occurrence of anemia in order to reduce its severity and frequency in the surgical candidates.

Materials & Methods: This cross-sectional analytical study aimed to explore the relationship between preoperative hemoglobin levels and the occurrence of moderate to severe postoperative anemia in TKR patients. The medical records of 242 TKA patients were reviewed. Demographic information, including age, gender, underlying conditions, and postoperative anemia status, was extracted and recorded in a checklist. Data were then entered into SPSS 27 for analysis.

Results & Discussion: The 242 patients included 204 (84.3%) women and 38 (15.7%) men, with mean age of 66.69 years (range: 37-84 years), and mean body mass index of 29.03 (20-44) kg/m². The anemia was based on second post-operative hemoglobin level. A pre-operative hemoglobin level of 13.15 mg/dl was identified as the best threshold to predict the high-risk patients, with a sensitivity of 73.6% and specificity of 72.6%.

Conclusion: Pre-operative hemoglobin level correlates with post-operative anemia in TKR surgery. A pre-operative hemoglobin below 75% is correlated with post-operative anemia.

Keywords: Total Knee Replacement, Anemia, Hemoglobins.

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Introduction

Hemoglobin (Hb) is a four-stranded iron-containing protein essential for oxygen (O_2) transport in mammals(1). Any condition that reduces the capacity or ability to transport O_2 results in anemia(2). Therefore, Hb serves as a critical parameter for diagnosing and evaluating anemia. The term "anemia," derived from the Ancient Greek word *anaimia*, meaning "lack of blood," broadly refers to a condition characterized by Hb levels below the normal range. The World Health Organization (WHO) has defined specific Hb thresholds for assessing anemia severity based on factors such as age, gender, ethnicity, altitude, smoking status, and pregnancy stages. Anemia is generally classified into three categories: mild (11–12.9 g/dL in men and 11–11.9 g/dL in women), moderate (8–10.9 g/dL), and severe (<8 g/dL). The most common cause of anemia is iron deficiency, often associated with poor nutrition, pregnancy, and menstruation in women. Vulnerable populations include children under five years of age, women of childbearing age, the elderly, and pregnant women. According to WHO studies, the prevalence of anemia in Iran is moderate (10–30%). A 2022 study by Dr. Zamani and colleagues, conducted on 161,686 individuals across 16 provinces, revealed the highest prevalence in Hormozgan Province (37.41%) and the lowest in Kurdistan Province (4.57%), with a prevalence rate of 21.5% in West Azerbaijan Province(3,4).

Anemia, particularly perioperative anemia, is a critical issue influenced over time by cultural norms, religious institutions, scientific advancements, and technological progress. Efforts to optimize outcomes have led to continuous evolution in its management. The first protocol for managing perioperative anemia, Patient Blood Management (PBM), was introduced in 1988 by Dr. James Isbister and later refined into WHO's Best Practice guidelines in 2014. These developments have influenced surgical practices, including the adoption of laparoscopic surgery, robotic-assisted surgery, and hospital- and lab-based digital algorithms supported by artificial intelligence and pre-existing datasets[5].

Postoperative anemia is a common occurrence in major surgeries, with a prevalence of 80–90%. It is often overlooked unless it necessitates blood transfusion. Understanding the factors contributing to postoperative anemia is key to its effective management. Perioperative anemia can impair oxygen transport, leading to tissue hypoxia and poor outcomes, with varying severity of complications. These include stroke, sepsis, infection, venous thromboembolism, impaired wound healing, prolonged hospitalization, reoperation, extended recovery time, myocardial infarction, and even cardiac arrest[6–9].

Given the high frequency of total knee arthroplasty surgeries, the lack of similar studies in Urmia and Iran, and the significance of this issue in improving patient outcomes, this study aimed to examine the relationship between preoperative hemoglobin levels and moderate to severe postoperative anemia in total knee arthroplasty patients.

The knee is the largest joint in the body, classified as a hinge joint, reliant on soft tissues for stability, and composed of two joints: the tibiofemoral and patellofemoral. It is also the most vulnerable joint, often requiring total knee replacement (TKR) surgery in cases of end-stage osteoarthritis, restricted movements, severe pain relief needs, significant mobility deficits, patellofemoral arthritis, malignancies, dislocations, fractures, etc. However, infections in the knee or other body parts, a non-functional extensor mechanism, and poor blood supply are contraindications for TKR surgery[10-12].

TKR is a major elective surgery with a high risk of bleeding, typically between 300-500 mL, necessitating a robust cardiovascular system to compensate for and tolerate blood loss up to 1000-1500 mL[9,13]. Introduced in the early 1970s, its use has increased with the rising prevalence of knee disorders. From 2008 to 2014, approximately 935,000 TKR surgeries were performed, and according to the American Joint Replacement Registry in 2022, 194,700 were primary cases, with projections for the U.S. reaching 1,230,000 annually by 2030[13-15]. Anemia is common around major surgery, with a prevalence of 30-40% preoperatively and 80-90% postoperatively[16,17].

Given these statistics, the importance of understanding the risk factors and causes of anemia is highlighted. Anemia post-surgery can be categorized into three groups based on timing: pre-operative, intra-operative, and post-operative.

Pre-operative factors

include gender (53% in women vs. 23% in men), age (increases with age), underlying diseases and coagulopathy, body mass index, medications (PPIs, metformin, anticoagulants, antiplatelet agents, etc.), natural anticoagulants (garlic, ginseng, etc.), drug interactions (rifampin, amiodarone, fluconazole, etc.), nutritional deficiencies, and the type and volume of intravenous fluids used (aiming to maintain normal blood volume to prevent excessive dilution, with colloids generally having more effect than crystalloids), weight, Body Surface Area (lower values correlate with higher anemia prevalence), preoperative hemoglobin (HB), and the American Society of Anesthesiologists (ASA) score (lower scores correlate with less bleeding).

Intra-operative factors

involve surgical duration, blood transfusion volume, surgical technique, use of drainage systems (which reduce intra-articular hematoma), blood loss amount, anesthesia method (neuraxial anesthesia can reduce peripheral blood flow and bleeding, improving the surgical field and reducing postoperative CRP), medications used (tranexamic acid, etc.), use of tourniquets (reducing surgery time and enhancing visibility), and blood management techniques (autologous blood donation, acute normovolemic hemodilution).

Post-operative factors

include drainage use, joint positioning (optimal flexion at 45 degrees for 48-72 hours), anticoagulant management, phlebotomy (which reduces hematocrit by 1.9% per 100 mL), and blood transfusions. Additionally, three factors are relevant across all phases: low body temperature (optimal range 33-37°C), acidosis, and hypocalcemia (calcium is essential for blood clotting). Among these, low preoperative hemoglobin, perioperative bleeding, and inadequate erythropoiesis due to increased inflammatory markers post-surgery are the primary independent causes of postoperative anemia[9,17-20].

About 1/3 of patients undergoing elective major surgery are anemic, with a linear relationship between hemoglobin levels and surgical complications; each unit decrease in hemoglobin increases the risk of surgical complications. The etiology of preoperative anemia can be multifactorial, but iron deficiency is the cause in 1/3 to 2/3 of these patients. Even among non-anemic patients, 1/3 might have iron deficiency, with causes varying by age and gender, but primarily due to nutritional deficiencies and chronic inflammation. In individuals over 65, UAA (Unexplained Anemia of Aging) is also significant, compounded by hormonal changes like decreased estrogen, TSH, IGF-1, etc. New oral drugs (HIF-PHIs) are approved in several countries for treating UAA and CKD[17,21].

Preoperative anemia is associated with increased blood transfusions, perioperative bleeding, morbidity, and mortality, leading to the development of a comprehensive, multidisciplinary strategy called Patient Blood Management (PBM), based on three pillars: 1) Identifying and treating preoperative anemia, 2) Reducing perioperative bleeding and coagulopathy, 3) Optimizing physiological tolerance to anemia.

Materials & Methods

1. Identification and Treatment of Anemia Before Surgery

Accurate etiological assessment to provide an appropriate therapeutic response is strongly recommended at this stage. Therefore, it is advised to evaluate Complete Blood Count (CBC) and an iron profile at least 4 weeks before surgery, or ideally 3 to 6 months in advance, to employ safer and more cost-effective methods (oral iron, erythropoietin-stimulating agents, either alone or in combination), and to identify cases requiring intravenous iron. However, due to patient pressure and insistence on expediting the surgical process, this has not always been implemented. Given the significance and sensitivity of this issue, it is recommended to assess CBC and iron profile up to 24 hours post-surgery (the time frame necessary for the increase in surgery-related inflammatory markers).

The Global Anemia Management Committee recommends that, as far as possible, a high-dose preparation for replacing iron stores should be prescribed.

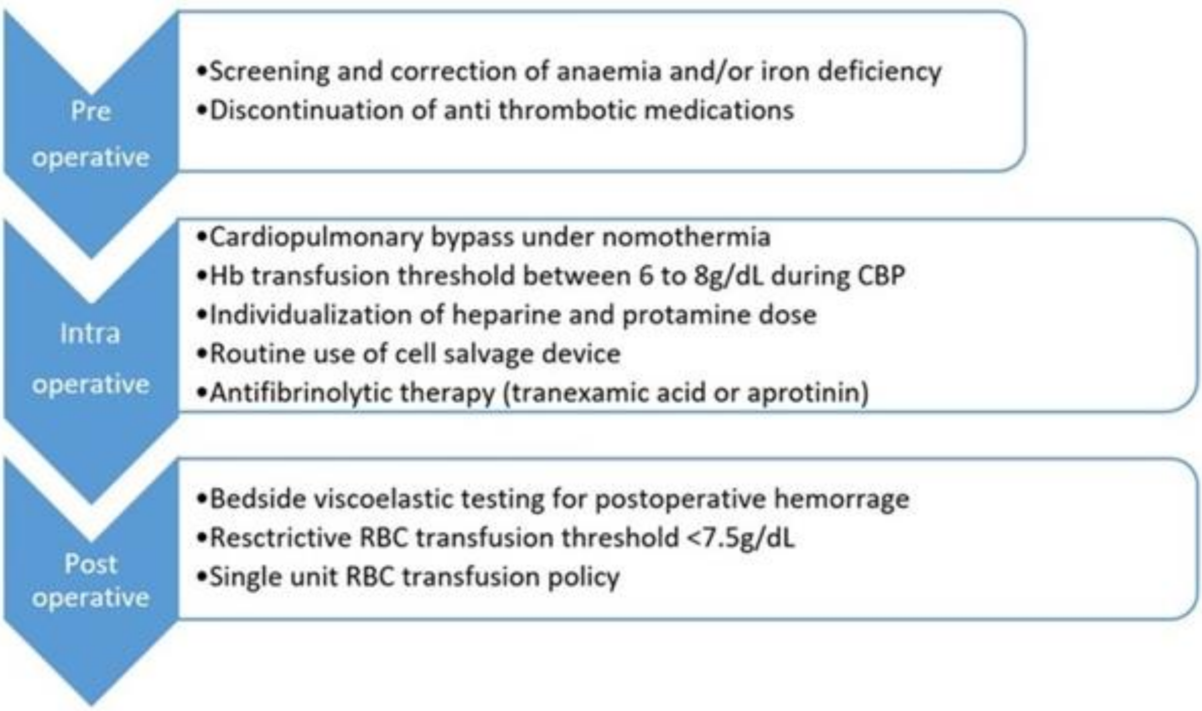


Figure 1: PBM Constituents

2. Reducing Bleeding and Coagulation Disorders Around Surgery

a. Preoperative Hemostasis Assessment and Management Around Surgery

Assessment of bleeding tendencies, bleeding-prone diseases, and history of medication use (anticoagulants), as well as family history of bleeding, should be prioritized over routine coagulation profile tests like Prothrombin Time (PT) and Partial Prothrombin Time (PTT). Recommendations include laboratory evaluations such as fibrinogen, PT, and PTT if anticoagulant drugs are used, and Platelet Function Analyzer (PFA-100) for suspected platelet disorders in surgeries with a high bleeding risk. Proper hemostatic drug management for patients on anticoagulants or for Venous Thromboembolism (VTE) prophylaxis has been shown to reduce perioperative bleeding. For instance, a study comparing the effects of three drugs - dalteparin (2500 IU), aspirin (100 mg), and rivaroxaban (10 mg) - administered from 12 hours post-TKR surgery up to 30 days, all groups received IV tranexamic acid (TXA). The study showed higher transfusion rates with dalteparin (20%) compared to aspirin (6.7%) and rivaroxaban (5%), with less blood drainage observed with aspirin (205.2 ± 69.0 mL) than rivaroxaban (243.4 ± 72.5 mL) and dalteparin (295.4 ± 72.5 mL)[22].

b. Surgical Techniques and Methods

In one study, the use of robotic-assisted TKR compared to conventional surgery did not significantly differ in postoperative hemoglobin levels[23]. Another study found that using cemented versus uncemented implants in TKR showed a significant difference (favoring uncemented implants) in outcomes and hemoglobin levels[24].

c. Use of Drugs to Reduce Bleeding

Medications like desmopressin and antifibrinolytics such as aprotinin, aminocaproic acid, and Tranexamic Acid (TXA) are used to reduce bleeding. Techniques to lower blood pressure either through anesthesia or regional hypotension at the surgical site are also employed. For example, intravenous and topical TXA has been associated with reduced bleeding and transfusion requirements without increasing the risk of DVT or Pulmonary Embolism (PE).

d. Real-Time Assessments During Surgery

Rapid, cost-effective assessments during surgery can lead to reduced blood transfusions and blood products, improving prognosis and reducing mortality up to 6 months post-surgery. Thromboelastography (TEG) is an example of such assessment tools.

e. Blood Transfusion Techniques

Techniques like cell salvage and Acute Normovolemic Hemodilution (ANH) are part of this strategy. The use of ANH has been shown to reduce allogeneic blood transfusion rates by up to 38%.

3. Suppression and Optimization of Physiological Tolerance to Anemia

The treatment of anemia through intravenous iron therapy, blood transfusion, and adjustment of the transfusion threshold—originally set at 10 g/dL and reduced to approximately 8 g/dL in non-cardiac patients—represents critical advancements in this field[16–18,20,21,25]. An extensive evaluation of Patient Blood Management (PBM) implementation on more than 600,000 cases across four major hospitals in Australia demonstrated remarkable outcomes: a 28% reduction in mortality, a 21% reduction in infections, a 31% reduction in cardiovascular events (such as stroke and myocardial infarction), a 15% reduction in hospital stay duration, a decrease in the prevalence of preoperative anemia from 21% to 14%, a reduction in preoperative transfusion thresholds from 7.9 g/dL to 7.3 g/dL, an increase in single-unit blood transfusion rates from 33% to 64%, a 41% reduction in overall blood transfusions, a 47% reduction in plasma transfusions, and a 27% reduction in platelet transfusions[26].

Given the high prevalence of total knee replacement (TKR) surgeries and the critical role of perioperative anemia, as well as the absence of similar studies in Urmia or other regions of Iran despite the widespread nature of this procedure in the province, the present study aimed to examine the relationship between preoperative hemoglobin (HB) levels and moderate to severe anemia in patients undergoing total knee arthroplasty.

In 2021, Cao G et al. conducted a study to identify risk factors associated with postoperative moderate to severe anemia (PMSA) and to determine the predictive value of preoperative hemoglobin (HB) levels for increased PMSA risk in total knee replacement (TKR) surgeries. Their investigation focused on the relationship between preoperative HB levels and PMSA in patients undergoing TKR. Their final conclusions highlighted that lower preoperative HB levels and greater intraoperative blood loss are independent risk factors for PMSA. In a study involving 474 TKR cases, the incidence of PMSA in primary TKR was 53.2%. Lower preoperative HB levels were significantly associated with PMSA, with an odds ratio (OR) of 1.138 (95% CI: 1.107–1.170, p < 0.001). Additionally, greater intraoperative blood loss was identified as a risk factor, with OR = 1.022 (95% CI: 1.484–4.598, p < 0.001). The optimal preoperative HB thresholds maximizing the area under the curve (AUC) were identified as 138.5 g/L for men (sensitivity: 79.4%, specificity: 75.0%) and 131.5 g/L for women (sensitivity: 74.7%, specificity: 80.5%)[25].

In 2022, Dhiman et al. conducted a study aimed at evaluating the prognostic value of preoperative hemoglobin (HB) concentrations in identifying patients at risk for severe postoperative anemia or requiring blood transfusions following total knee replacement (TKR). The study analyzed the application of preoperative HB levels to guide postoperative blood tests in TKR patients using decision curve analysis. Data from 2011 to 2018 on 2,363 TKR cases were examined.

The findings indicated that the likelihood of patients experiencing postoperative HB levels below 7–8 g/dL or requiring allogeneic blood transfusions decreases with each unit increase in preoperative HB. Specifically, for every one-unit increase in preoperative HB, the odds of requiring allogeneic transfusions were reduced by 8% (OR = 0.92, 95% CI: 0.90–0.94)[27].

In 2022, Yash Chaudhri et al. investigated predictors of postoperative hemoglobin (HB) levels below 8 g/dL and the associated outcomes with and without blood transfusion in total knee replacement (TKR) surgeries performed under a multi-faceted blood management protocol from 2017 to 2018. They analyzed 1,583 TKR cases and compared pre- and postoperative variables between patients with postoperative HB below and above 8 g/dL.

Logistic regression and receiver operating characteristic (ROC) curves were employed to assess predictors of postoperative HB below 8 g/dL. Key findings include:

Positive predictors of postoperative HB below 8 g/dL:

- Lower preoperative HB levels: A 1 g/dL reduction in preoperative HB increased the odds by 2.1 (OR = 2.1, 95% CI: 1.3–3.4).
- Longer operative times: For every 30-minute increase in operative duration, the odds increased by 2.0 (OR = 2.0, 95% CI: 1.6–2.6).

Negative predictors of postoperative HB below 8 g/dL:

- Use of tranexamic acid (OR = 0.42, 95% CI: 0.20–0.85).
- Higher body mass index (BMI): For every 1 kg/m² increase, the odds decreased by 0.90 (OR = 0.90, 95% CI: 0.86–0.94).

The best thresholds for predicting postoperative HB below 8 g/dL were:

- HB below 12.4 g/dL in women.
- HB below 13.4 g/dL in men.

Overall, 5.2% of patients with postoperative HB levels between 7–8 g/dL and 95% of those with HB below 7 g/dL received blood transfusions. Patients with postoperative HB below 8 g/dL had longer hospital stays (p < 0.001), higher rates of emergency department visits or readmissions (p = 0.001), and greater incidence of acute kidney injury (p < 0.001). Among patients with HB below 8 g/dL, those who received blood transfusions had significantly lower HB levels (p < 0.001) and longer hospital stays (p = 0.035) than those who did not receive transfusions[28].

Wu EB et al. (2022) aimed to identify risk factors associated with significant bleeding in TKR and determine whether these risk factors are modifiable. They conducted a retrospective cohort study from January 2009 to December 2015, dividing patients into two groups: Group A included patients with an HB drop of ≤2 g/dl, and Group B included patients with an HB drop of more than 2 g/dl. The analyzed factors included gender, age, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, comorbidities, preoperative platelet count, use of tranexamic acid (TXA), operation time, and type of anesthesia. In total, 3,350 patients met the analysis criteria, with 1,782 in Group A and 1,568 in Group B. Five independent risk factors for significant bleeding were identified: male gender (OR=1.29, 95% CI=1.08-1.53, p=0.005), age (OR=1.02, 95% CI=1.01-1.03, p=0.001), use of TXA (OR=0.39, 95% CI=0.34-0.45, p<0.001), spinal anesthesia compared to general anesthesia (OR=0.71, 95% CI=0.56-0.90, p=0.004), and preoperative platelet count (OR=0.96, 95% CI=0.93-0.98, p=0.001). Among these identified risk factors, preoperative platelet count, use of TXA, and spinal anesthesia were modifiable. These potentially adjustable risk factors should be considered during intraoperative care and anesthetic planning by surgeons and anesthesiologists, particularly for patients at risk of significant bleeding[29].

Ryan SP et al. (2019) aimed to identify risk factors associated with postoperative blood transfusion and establish a preoperative HB threshold in total knee replacement (TKR) surgery to identify patients who could benefit from blood conservation programs. Patient demographics and preoperative hemoglobin levels, along with intraoperative and postoperative variables such as transfusion rates, were determined. Patients were classified based on whether they received a transfusion after surgery, and risk factors were identified through univariate and multivariate analyses. Optimal cut-off values for HB were determined by simultaneously maximizing sensitivity and specificity for predicting the risk of a postoperative transfusion event. Men and women were analyzed independently. A total of 532 patients undergoing TKR were analyzed, with 33 patients (6.2%) requiring blood transfusion. Older age (p=0.019), lower preoperative HB levels (p<0.001), and not receiving tranexamic acid (p<0.001) were associated with an increased risk of postoperative transfusion. A preoperative HB level of 12.5 g/dl, with a sensitivity of 84.8% and specificity of 76.4%, was identified as the optimal cut-off for predicting postoperative transfusion needs in all patients. Preoperative anemia, despite current antifibrinolytic treatments, remains a predictor of transfusion following TKR. Patients with preoperative HB levels below 12.5 g/dl who do not receive intravenous tranexamic acid are particularly at risk and should be considered for blood conservation programs[30].

Mathew KK et al. (2020) investigated whether iron deficiency anemia (IDA) is a risk factor for poorer outcomes in total knee replacement (TKR) surgery. They examined its effect on (1) hospital length of stay, (2) 90-day readmissions, (3) healthcare costs, (4) medical complications, and (5) implant-related complications. The study identified and matched patients with and without IDA undergoing TKR using a nationwide administrative database, which included 94,053 patients with IDA and 470,264 patients without IDA. Primary outcomes, statistically analyzed, included hospital length of stay, readmission rates, care costs, medical complications, and implant-related complications. Patients with IDA had significantly longer hospital stays (4 days vs. 3 days; p < 0.0001), higher 90-day readmission rates (25.8% vs. 16.3%; OR = 1.77; p < 0.0001), higher surgical costs ($13,079.42 vs. $11,758.25; p < 0.0001), and higher total 90-day global care costs ($17,635.13 vs. $14,439.06; p < 0.0001) compared to patients without IDA. Moreover, patients with IDA showed significantly higher rates and odds of medical complications (3.53% vs. 1.33%; OR = 2.71; p < 0.0001) and implant-related complications (3.80% vs. 2.68%; OR = 1.43; p < 0.0001) resulting from TKR. In their final conclusions, the authors stated that patients with IDA had poorer outcomes across all measured parameters[31].

Methodology

This study is a cross-sectional analytical investigation aimed at examining the relationship between preoperative hemoglobin levels and moderate to severe anemia in patients undergoing total knee arthroplasty (TKA). After obtaining patient consent for participation, all patients undergoing TKA, confirmed through medical documentation, who referred to the orthopedic department of Imam Khomeini Educational and Medical Center, were included in the study. Blood samples were collected from patients, and serological tests were performed. Hemoglobin levels between 8-11 g/dL were classified as moderate anemia, and levels below 8 g/dL were classified as severe anemia.

The surgical approach for all patients involved medial parapatellar arthrotomy with the use of a pneumatic tourniquet. No intravenous or local tranexamic acid was administered to any of the patients.

Descriptive characteristics of the patients were presented using frequency tables, charts, and descriptive statistics, including mean and standard deviation. The McNemar test was used to compare the frequency of moderate to severe anemia before and after surgery, considering age and sex distribution. The optimal threshold for diagnosing postoperative anemia was determined using the ROC curve, and data analysis was conducted using SPSS version 27. This study commenced following ethical approval from the university's ethics committee under the code IR.UMSU.HIMAM.REC.1402.059. Only the information necessary for conducting the study was collected, and no additional data were extracted. No costs were imposed on the patients, and results were recorded in group format, without individual or identifiable patient information being registered.

Descriptive characteristics of the patients were presented in the form of frequency tables and charts, along with descriptive statistics (mean and standard deviation). Hemoglobin levels below 8 g/dL were considered as severe anemia, 8 to 11 g/dL as moderate anemia, and above 11 g/dL as mild anemia. In determining the diagnostic value (accuracy) of preoperative hemoglobin in predicting postoperative anemia in the present study, the optimal threshold was identified using the ROC curve. Given the low number of severe anemia cases, moderate and severe anemia cases were categorized based on postoperative Hb levels, with those above 11 g/dL considered mild. The ROC curve for preoperative hemoglobin, along with the reference line, was plotted to assess its accuracy in diagnosing anemia on the first and second day after surgery in the patients under study. The area under the ROC curve represents the test's accuracy (in this study, preoperative hemoglobin), and a value above 50% is considered acceptable. Data analysis was conducted using SPSS version 26, and a p-value of less than 5% was considered statistically significant.

Results

Table 1 shows the gender distribution of the patients under study. Among the patients who underwent surgery during the study period, 204 were female (84.3%) and 38 were male (15.7%).
Table 2 presents the age distribution, body mass index (BMI), and laboratory findings of the patients under study. The mean age of the patients was 66.69 years (range 37 to 84 years), and the mean BMI was 29.03 kg/m² (BMI range 20 to 44 kg/m²).
Table 3 compares the frequency of moderate to severe anemia on the first day post-surgery in relation to the gender distribution. Among the 38 male patients, 76.3% (29 patients) had mild anemia postoperatively, whereas the same proportion was 47.1% (96 patients) among the 204 female patients. The frequency of moderate anemia, based on hemoglobin levels, was higher in women (112 patients, 51.5%) than in men (9 patients, 23.7%). The correlation between the severity of anemia and gender distribution was statistically significant (P = 0.004). Table 4 compares the frequency of moderate to severe anemia on the second day post-surgery in relation to the gender distribution. Among the 38 male patients, 71.1% (27 patients) had mild anemia postoperatively, whereas 42.2% (96 patients) of the 204 female patients had mild anemia. The frequency of moderate anemia was higher in women (114 patients, 55.9%) compared to men (11 patients, 28.9%). Severe anemia was observed in 2 patients on the second day post-surgery. The correlation between the severity of anemia and gender distribution was statistically significant (P = 0.004).
Table 5 compares the frequency of moderate to severe anemia on the first day post-surgery based on age distribution. The mean age of patients with moderate and mild anemia was similar, while patients with severe anemia were younger. However, there was no statistically significant difference between the patients based on the severity of anemia (P = 0.18). Table 6 compares the frequency of moderate to severe anemia on the second day after surgery based on age distribution. The mean age of patients with moderate anemia was higher than that of other patients, while the age of those with severe and mild anemia was similar. However, there was no statistically significant difference between the patients based on the severity of anemia (P = 0.31).
Among the 242 patients under study, 184 had no underlying diseases (76%), 7 had a history of inflammation (2.9%), 36 had metabolic diseases (14.9%), and 15 had cardiovascular diseases (6.2%).
Table 7 compares the frequency of moderate to severe anemia on the first day post-surgery based on underlying diseases. None of the patients with cardiovascular, metabolic, or inflammatory diseases had severe anemia, and more than half of the patients with cardiovascular diseases and no underlying conditions had mild anemia on the first day post-surgery. Most patients with metabolic and inflammatory diseases had moderate anemia on the first day post-surgery. However, there was no statistically significant difference between the patients with different underlying diseases in terms of anemia severity (P = 0.38).

Table 1: Gender distribution of the patients under study

Gender	Frequency	Percentage (%)
Female	204	84.3
Male	38	15.7

Table 2: Age, body mass index, and laboratory findings of the patients under study

Variable	Minimum	Maximum	Standard Deviation	Mean
Body mass index (kg/m²)	20	44	5.12	29.03
Age (years)	37	84	7.16	66.69
Preoperative hemoglobin	9.3	16.9	1.45	13.05
Day 1 postoperative hemoglobin	6.8	15.8	1.49	11.25
Day 2 postoperative hemoglobin	7.4	15.2	2.62	11.2
Day 1 postoperative hematocrit	19.71	44.9	5.25	35.17
Day 2 postoperative hematocrit	23.2	45.2	7.63	32.93

Table 3: Frequency distribution of anemia severity on the first day after surgery by gender

Anemia Severity	Male (n=38)	Female (n=204)	P value*
Severe	0	3 (1.5%)	
Moderate	9 (23.7%)	105 (51.5%)	0.004
Mild	29 (76.3%)	96 (47.1%)	

*Fisher's Exact Test

Table 4: Frequency distribution of anemia severity on the second day after surgery by gender

Anemia Severity	Male (n=38)	Female (n=204)	P value*
Severe	0	2 (4%)	
Moderate	11 (28.9%)	114 (55.9%)	0.004
Mild	27 (71.1%)	86 (42.2%)	

*Fisher's Exact Test

Table 5: Age distribution based on anemia severity on the first day after surgery

Age	Anemia Severity	Mean Age	Standard Deviation	Min Age	Max Age	P value*
Severe	67.62	5.8	53	69		
Moderate	67.51	6.06	49	82	0.18	
Mild	66.04	7.98	37	84		

*Kruskal-Wallis Test

Table 6: Age distribution based on anemia severity on the second day after surgery

Age	Anemia Severity	Mean Age	Standard Deviation	Min Age	Max Age	P value*
Severe	65	8.34	53	72		
Moderate	67.41	6.24	49	83	0.31	
Mild	65.69	8.03	37	84		

*Kruskal-Wallis Test

Table 7: Frequency distribution of anemia severity on the first day after surgery based on underlying diseases

Underlying Disease	Anemia Severity	Cardiovascular	Metabolic	Inflammatory	No Underlying Disease	P value*
Severe	0	0	0	3 (6.1%)		
Moderate	7 (46.7%)	23 (63.9%)	4 (57.1%)	80 (43.5%)		0.38
Mild	8 (53.3%)	13 (36.1%)	3 (42.9%)	101 (54.9%)		

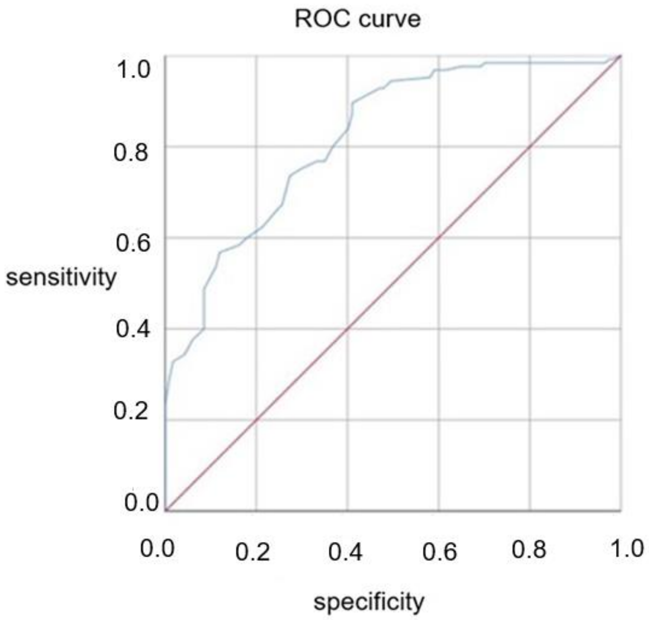
*Fisher's Exact Test

Table 8 compares the frequency of moderate to severe anemia on the second day after surgery based on underlying diseases. No severe anemia was reported in patients with cardiovascular, metabolic, or inflammatory diseases. More than half of the patients in all three underlying disease categories had moderate anemia on the second day post-surgery, and there was no statistically significant difference in anemia severity among patients with different underlying diseases (P = 0.54). On the first day after surgery, out of 242 patients, 117 had moderate to severe anemia (48.3%), and 125 had mild anemia (51.7%). Based on this, the diagnostic value (accuracy) of preoperative hemoglobin in detecting anemia on the first day after surgery was calculated. Figure 2 shows the ROC curve for preoperative hemoglobin along with the reference line in detecting anemia on the first day after surgery in the patients under study. The area under the ROC curve based on the presence of anemia (moderate and severe) on the second day after surgery was 0.82. It appears that the preoperative hemoglobin level in detecting anemia on the first day after surgery is acceptable for the patients studied, and this interpretation was statistically significant (P < 0.001).

Considering the diagnosis of anemia on the first day after surgery (Gold Standard), the best cutoff point for identifying high-risk patients for anemia based on preoperative hemoglobin was 13.85 mg/dL (with sensitivity and specificity of 53.6% and 46.4%, respectively). Hemoglobin levels below 13.85 mg/dL indicate that the patients are at lower risk for postoperative anemia. However, the sensitivity and specificity are lower when determining anemia on the second day after surgery.

Table 8: Frequency distribution of anemia severity on the second day after surgery based on underlying diseases

Underlying Disease	Anemia Severity	Cardiovascular	Metabolic	Inflammatory	No Underlying Disease	P value*
Severe	0	0	0	4 (2.2%)		0.54
Moderate	8 (53.3%)	24 (66.7%)	4 (57.1%)	89 (48.4%)		
Mild	7 (46.7%)	12 (33.3%)	3 (42.9%)	91 (49.5%)		
*Fisher's Exact Test						



P value	95% Confidence Interval	Area under the ROC curve
<0.001	0.769 - 0.872	0.82

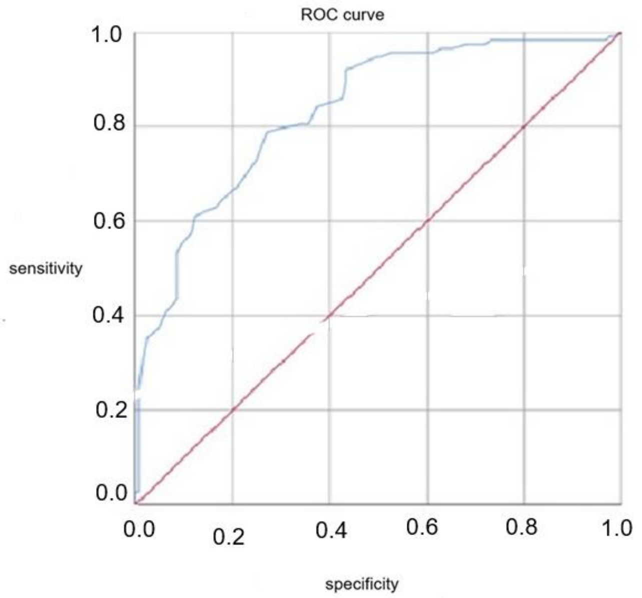
Figure 2: ROC Curve of Preoperative Hemoglobin in Diagnosing Postoperative Day 1 Anemia in the Studied Patients

On the second day after surgery, of the 242 patients, 129 had anemia (moderate and severe) and 113 had mild anemia (53.3% and 46.7%, respectively). Based on this, the diagnostic value (accuracy) of preoperative hemoglobin in detecting anemia on the second day after surgery was calculated. Figure 3 shows the ROC curve for preoperative hemoglobin, along with the reference line, in detecting anemia on the second day after surgery in the patients under study. The area under the ROC curve for detecting anemia (moderate and severe) on the second day after surgery was 0.83. It appears that preoperative hemoglobin levels are acceptable for detecting anemia on the second day after surgery in the patients studied, and this interpretation is statistically significant (P < 0.001).

Considering the diagnosis of anemia on the second day (gold standard) after surgery, the best cutoff point for identifying high-risk patients based on preoperative hemoglobin was 13.15 mg/dL (sensitivity and specificity of 73.6% and 72.6%, respectively). Hemoglobin levels below 13.15 mg/dL in the patients under study are associated with a higher risk of postoperative anemia. It appears that preoperative hemoglobin has higher sensitivity and specificity in differentiating patients based on the presence of anemia on the second day after surgery compared to the first day after surgery.

Discussion

Anemia remains a major public health issue in many Asian countries, and targeted interventions for at-risk populations are recommended[1]. Moderate to severe anemia after orthopedic surgeries significantly affects a considerable proportion of Total Knee Replacement (TKR) patients, and a notable decrease in hemoglobin levels following hip arthroscopy has also been reported[2]. The prevalence of anemia in Iranian patients undergoing orthopedic surgeries has been reported to be as high as 53.2%, and low preoperative hemoglobin levels can be an important risk factor for this anemia, often requiring blood transfusion[3,4]. Orthopedic surgery patients, including those undergoing total hip and knee replacement, are generally older than 50 years, with most patients suffering from underlying conditions such as hypertension, diabetes, and heart disease. Additionally, women are more likely to experience anemia, and these pre-existing conditions place orthopedic surgery patients at higher risk for developing anemia[4]. In such cases, routine control and necessary preventive measures are essential to prevent postoperative anemia and its associated complications, such as major cardiac events[6].



P value	95% Confidence Interval	Area under the ROC curve
<0.001	0.782-0.883	0.83

Figure 3: ROC curve for preoperative hemoglobin in detecting anemia on the second day after surgery in the patients under study.

On the other hand, identifying a cutoff point to distinguish high-risk and low-risk patients for postoperative anemia based on preoperative hemoglobin levels could provide surgeons with opportunities to treat anemia before surgery. Early interventions, such as erythropoietin and iron supplementation, can reduce the risk of postoperative anemia and prevent complications[7-9].
This study aimed to determine the relationship between preoperative hemoglobin and moderate to severe anemia in total knee replacement (TKR) patients at Imam Khomeini Hospital, Urmia. Based on moderate to severe postoperative anemia and the absence of anemia after surgery as the gold standard, the diagnostic value of preoperative hemoglobin for detecting anemia and the best cutoff point for identifying high-risk TKR patients for anemia were determined.
On the first day after surgery, 48.3% of the patients had moderate to severe anemia, and the diagnostic accuracy of preoperative hemoglobin for detecting anemia on the first postoperative day was acceptable (area under the curve = 0.82). The best cutoff point for identifying high-risk patients based on preoperative hemoglobin was 13.85 mg/dL. In our study population, hemoglobin levels below 13.85 mg/dL are associated with a higher risk of postoperative anemia.
On the second day after surgery, 53.3% of the patients had moderate to severe anemia, and the diagnostic accuracy of preoperative hemoglobin for detecting anemia on the second postoperative day was also acceptable (area under the curve = 0.83). The best cutoff point for identifying high-risk patients based on preoperative hemoglobin was 13.15 mg/dL. In our study population, hemoglobin levels below 13.15 mg/dL indicate a higher risk of postoperative anemia. Furthermore, the preoperative hemoglobin level had higher sensitivity and specificity in distinguishing patients based on anemia on the second day after surgery compared to the first day.
It is important to note that no other studies within the country were found in the databases for comparison with our findings, and the results were compared with those from studies conducted in other countries.
The lowest hemoglobin level on the second day after surgery in our study was observed in a 40-year-old female patient with a preoperative hemoglobin of 11.2 g/dL, which decreased to 6.2 g/dL on the second day. This drop could be due to the prolonged duration of her surgery and the significant amount of intravenous fluids administered during and on the first postoperative day (progressive anemia).
In the study by Kolin DA and colleagues, the area under the curve for preoperative hemoglobin in detecting postoperative anemia was 0.88, and the area under the curve for predicting the need for blood transfusion postoperatively was 0.9, indicating a strong diagnostic value for preoperative hemoglobin[10]. Similarly, in the study by Cao G and colleagues in China, which was conducted on TKR patients similar to ours, 53.2% of patients developed moderate to severe anemia, and the area under the ROC curve was reported as similar to our findings. The predictive cutoff values for postoperative anemia were 138.5 g/L for men and 131.5 g/L for women, which were statistically significant and supported their clinical application[5].
In the study by Valbuena I and colleagues in Spain, a preoperative hemoglobin level below 13 g/dL significantly increased the likelihood of requiring allogenic blood transfusion (ABT) and prolonged hospital stays[4]. This finding emphasizes the need for preoperative screening and anemia management before surgery, particularly for patients at risk for anemia. These patients often do not exhibit clinical symptoms of anemia or bleeding, which should be considered preoperatively. As Harris AB and colleagues demonstrated in their study in Canada, TKR patients with preoperative anemia who did not receive supportive blood transfusions had higher rates of complications, such as prolonged hospital stays, mortality, hospital infections, and other adverse outcomes. This highlights the importance of preoperative anemia management in identifying TKR patients at high risk for postoperative anemia[10].
It is important to note that preoperative hemoglobin cutoff values for predicting acute events, such as levels below 13 g/dL, have been reported. In a study conducted in China, for patients aged over 80 with pelvic fractures, preoperative hemoglobin levels below 10 g/dL were associated with increased postoperative cardiac complications[6].
In our study, the majority of patients were female, which aligns with the findings of Cao G and colleagues in China. This could contribute to a reduction in the accuracy of identifying risk factors and predicting the preoperative cutoff value for anemia in the general patient population, including both males and females. It is suggested that future studies with larger sample sizes, including an equal proportion of males

and females, will enable the generalization of the selected cutoff point to differentiate by gender in TKR patients. Moreover, the retrospective nature of our study presents limitations, which are inherent in all similar studies[5].

Another important point that must be considered alongside the aforementioned characteristics is that the best cutoff point is not always the one with the highest sensitivity and specificity. For example, in our study, if the doctor wants to select the optimal cutoff point using preoperative anemia to avoid missing any high-risk patients, it may lead to delayed treatments and potential complications. By lowering the cutoff point, false negatives are reduced, but this increases false positives. Therefore, in such situations, the optimal point should first be identified, and then the positivity threshold can be slightly lowered. However, caution is needed to ensure that increasing sensitivity does not excessively decrease specificity[12,13].

Recommendations

Based on the search of accessible databases, no similar studies have been conducted on the use of preoperative anemia in predicting postoperative anemia in Iranian patients. Therefore, it seems necessary to conduct further studies aimed at improving the sensitivity and specificity for Iranian patients, making it possible to generalize the findings to this population. Future research should investigate specific subgroups, such as those with various underlying conditions, to identify any changes in diagnostic accuracy.

Conclusion

As seen in our study and similar studies conducted in other countries, prediction models based on preoperative anemia for evaluating postoperative anemia and the need for blood transfusions have shown high accuracy. Additionally, the suggested cutoff values in our study were similar to those found in other studies, indicating that preoperative hemoglobin levels can serve as a reliable predictor for the development of anemia after surgery in TKR patients. In most of these studies, the area under the curve was above 75% and even above 80%, which is considered both clinically acceptable and statistically significant. Therefore, preoperative evaluation and the presence of anemia in TKR patients can be useful for identifying high-risk patients and making clinical decisions.

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