

Anaemia is Associated with Increased Postoperative Morbidity and Decreased Overall Survival in Patients with Colorectal Cancer

Ali Farsi, MBBS, MAdvSurg* Maha Asiri**, Halah Almansi***, Hatem Alahwal, MBBS, FRCPC, MPH***** Sara Farsi, MBBS, MMedEd***** Nora Trabulsi, MBBS* Mohammed Nassif, MBBS* Ahmad Khoja, MBBS***** Alaa Habeebullah, MBBS***** Afnan Jiffri, MBBS***** Ghada Enani, MBBS, Med, FRCSC* Nouf Akeel, MBBS* Omar Iskanderani, MBBS, DES*****

ABSTRACT

Anaemia is a common comorbidity in colorectal cancer (CRC), often resulting from tumour-related blood loss, nutritional deficiencies, and chronic inflammation. Anaemia is associated with reduced survival and a higher incidence of perioperative complications, yet its independent prognostic significance remains uncertain. This study aimed to evaluate the impact of anaemia on short- and long-term outcomes in patients undergoing surgery for CRC. This retrospective cohort study included 311 patients who underwent surgery for CRC. Baseline demographic, clinical, and surgical characteristics were recorded. Anaemia was defined by preoperative haemoglobin levels. Surgical outcomes included postoperative complications, 30-day mortality, and recurrence. Survival outcomes were analysed using Kaplan–Meier estimates. Cox proportional hazards regression identified independent predictors of recurrence and poor outcomes (recurrence or mortality). Statistical significance was determined at $p > 0.05$. Anaemia was present in 51.4% of 311 patients (mean age 58 years) with CRC, with 22.5% requiring emergency surgery and 16.4% receiving perioperative transfusion. Mortality within 30 days occurred in 11 cases (3.5%); anastomotic leak was observed in 13.0% of 247 patients with anastomosis. The overall rate of postoperative complications was 27.0%. Patients with anaemia had significantly higher rates of postoperative complications (33.8% vs 19.9%, $p = 0.006$) and troponaemia (17.5% vs 9.3%, $p = 0.034$). Anaemia reduced overall survival ($p = 0.021$) but did not impact recurrence ($p = 0.368$) or recurrence-free survival ($p = 0.123$). Preoperative anaemia is common among patients with CRC and was associated with increased short-term postoperative complications and reduced overall survival in univariate analysis. While anaemia was not an independent predictor of recurrence or long-term mortality in multivariate analysis, early identification and intervention may improve perioperative outcomes.

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- * Department of Surgery, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.
E-mail: alihmfarsi@gmail.com
- ** Faculty of Medicine, King Abdulaziz University
Jeddah, Saudi Arabia.
- *** Faculty of Medicine, Ibn Sina National College
Jeddah, Saudi Arabia.
- **** Department of Hematology, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.
- ***** Hematology Research Unit, King Fahd Medical Research Centre
King Abdulaziz University, Jeddah, Saudi Arabia.
- ***** Department of Anesthesia and Critical Care
King Abdulaziz University Hospital, King Abdulaziz University
Jeddah, Saudi Arabia.
- ***** Department of Surgery, Faculty of Medicine
King Abdulaziz University, Rabigh, Saudi Arabia.
- ***** Thoracic Surgery Division, Department of Surgery
Faculty of Medicine, King Abdulaziz University
Jeddah, Saudi Arabia.
- ***** Department of Surgery, King Abdullah Medical Complex
Jeddah, Saudi Arabia.
- ***** Department of Radiology, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.

INTRODUCTION

Anaemia is a condition characterised by insufficient numbers of healthy red blood cells or haemoglobin, reducing the blood's capacity for oxygen transport to tissues. This results in symptoms such as fatigue, weakness, dizziness, and shortness of breath. Haemoglobin, an iron-rich protein in red blood cells, binds oxygen in the lungs and transports it throughout the body. Anaemia is diagnosed when haemoglobin levels fall below 13.5 g/dl in men or 12.0 g/dl in women^{1,2}.

Anaemia can be classified as mild (10.0 g/dl to lower normal limit), moderate (8.0–10.0 g/dl), severe (6.5–7.9 g/dl), or life-threatening (below 6.5 g/dl) based on haemoglobin levels. Anaemia can be acute, often due to sudden blood loss or rapid red blood cell destruction, or chronic, commonly caused by nutritional deficiencies, chronic illnesses, or hereditary conditions².

Anaemia is highly prevalent globally, particularly in lower-income countries where it contributes significantly to healthcare burdens. Preoperative anaemia is common in patients undergoing elective colorectal surgery, often due to tumour-induced blood loss and inflammation. Around 13.9% of patients are affected, with iron deficiency and chronic diseases being the most common causes³. Anaemia has an even greater prevalence in patients with cancer: those diagnosed are five times more likely to have anaemia than healthy individuals. Risk factors include metastatic disease and nutritional deficiencies, particularly iron, B12, and folate⁴.

Anaemia is a significant risk factor in colorectal surgery, influencing both short- and long-term outcomes. In the short term, it is associated with higher rates of postoperative complications, including infections, sepsis, cardiac events, increased need for red blood cell transfusions, and prolonged hospital stays, all of which contribute to a greater healthcare burden^{3,5-7}.

In the long term, preoperative anaemia serves as a predictor for reduced overall and disease-free survival, increased local recurrence, and high-risk disease. These associations are consistently observed in rectal cancer but are less evident in colon cancer; distant recurrence appears unaffected. Preoperative anaemia – regardless of severity – is independently associated with higher morbidity and mortality, as well as more advanced tumour stages in patients with colorectal cancer (CRC)⁸⁻¹².

Additionally, patients with anaemia often require allogeneic blood transfusion (ABT), which is associated with worse outcomes in CRC surgery. ABT increases the risk of cancer-related mortality, recurrence, metastasis, postoperative infections, and longer hospital stays¹³. This emphasises the importance of early anaemia prevention, promoting anaemia tolerance, and limiting ABT use in improving outcomes¹⁴. Early interventions such as preoperative intravenous (IV) iron supplementation can effectively reduce complications and enhance recovery^{4,7}.

The aim of this study was to evaluate the short- and long-term effects of anaemia on patients with CRC undergoing surgery at a tertiary care academic institute.

METHODS

Approval was obtained from the Unit for Biomedical Ethics at King Abdulaziz University (reference number 23-26). A retrospective chart review was performed. All files for patients undergoing colorectal surgery from 2013–2020 were reviewed for a diagnosis of colon

adenocarcinoma. Both emergent and elective operations were included. Baseline demographics such as age, gender, laboratory values, and the need for preoperative transfusion were extracted from the files. Operative details such as surgical technique, blood loss, and the need for transfusion in the operating room were also obtained. Charts detailing the patients' pathologic stages were reviewed; all patients with Stage 1–4 disease and those with a complete pathologic response were included. The patients' postoperative course was evaluated, specifically regarding mortality and morbidity in the first 30 days, the need for postoperative transfusion, length of hospital and intensive care unit stay, and cancer recurrence and survival. Patients were contacted by telephone to confirm survival or recurrence where 5-year follow-up data were unavailable.

Data analysis: Data from Microsoft Excel worksheets were imported into SPSS version 27.0 (IBM SPSS Inc., Armonk, NY, USA) for further statistical analysis. Normality of the data was determined using the Shapiro–Wilk test. Normally distributed continuous variables were presented as mean $\pm$ S.D and compared using the student's T-test. Non-normally distributed continuous variables were presented as median (IQR) and compared using the Mann–Whitney U test. Categorical variables were presented as frequencies and percentages and compared using the chi-square test. Fisher's exact test was applied where the expected cell count in one or more cells was less than 5.

The prevalence of anaemia was recorded and surgical outcomes were compared in patients with and without anaemia using appropriate statistical tests as described. Kaplan–Meier curves were constructed to determine the association between anaemia and disease recurrence, recurrence-free survival, and overall survival.

Cox proportional hazards regression models were constructed and hazard ratios (HR) were calculated with 95% confidence intervals to determine the association of various predictors with recurrence, poor outcome (recurrence or mortality), and mortality. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 311 patients (mean age 58 ± 15 years) who underwent CRC surgery were included in this study. Of these, 179 (57.6%) were male. Anaemia was present in 53.6% of males and 48.5% of females. Preoperative PRBC transfusion was administered in 51 (16.4%) cases. Rectal involvement was observed in 39.2% of cases, left-sided colonic tumours in 31.2%, and right-sided colonic tumours in 29.6%. Stage 3 tumours were most common (present in 35.4% of patients). Patient baseline demographic and clinical characteristics are summarised in Table 1.

Emergency surgery was required in 70 (22.5%) cases. Low anterior resection was the most commonly performed surgery (27.0%), followed by right hemicolectomy (22.5%) and sigmoid resection (22.2%). Procedures were performed laparoscopically in 127 (40.8%) patients. Chemotherapy was administered in 182 (58.5%) cases; radiotherapy was administered in 76 of 122 cases (62.3%) with rectal involvement. Patient surgical characteristics are summarised in Table 2.

The mean perioperative blood loss was 382 ± 399 ml. The mean postoperative hospital stay was 15 ± 19 days and length of monitored (ICU) care was 2 ± 4 days. Only 2 (0.6%) patients experienced stroke within 30 days. Mortality within 30 days occurred in 11 (3.5%) cases. Of the 247 patients with anastomosis, anastomotic leak was observed in 32 (13.0%) cases. Presence of one or more postoperative complications was reported in 84 (27.0%) patients.

Cancer recurrence (both local and distant) was observed in 36 (11.6%) patients. Overall, 2.9% patients had recurrence within 1 year, 7.1% within 3 years, and 9.6% within 5 years of surgery. Postoperative complications at 30 days included stroke in 0.06% of patients, mortality in 3.5%, troponaemia in 13.5%, DVT in 1.0%, PE in 2.6%, positive blood cultures in 5.1%, and UTI in 17.7%; anastomotic leak occurred in 13.0% of patients with anastomosis.

The comparison of surgical outcomes between patients with and without anaemia showed that the incidence of postoperative complications (including UTI, DVT, PE, sepsis, and MI) was higher in patients with anaemia (33.8% vs 19.9%, $p = 0.006$); troponaemia was also more

common (17.5% vs 9.3%, $p = 0.034$). Other variables such as duration of surgery ($p = 0.140$), length of hospital stay ($p = 0.143$), duration of monitored care ($p = 0.054$), 30-day stroke incidence ($p = 0.967$), 30-day mortality ($p = 0.410$), ER visit in the first year ($p = 0.488$), and recurrence ($p = 0.379$) did not show a statistically significant association with anaemia (Table 3).

Survival analysis using Kaplan–Meier curves showed that anaemia significantly reduced overall survival in patients undergoing CRC surgery ($p = 0.021$). There was no statistically significant effect of anaemia on recurrence ($p = 0.368$) and recurrence-free survival ($p = 0.123$). Figures 1–3 depict Kaplan–Meier curves showing the effect of

Table 1. Baseline demographic and clinical characteristics of patients with colorectal cancer (N = 311)

Characteristic	Mean $\pm$ S.D	Minimum	Maximum
Age (years)	58 $\pm$ 15	23	99
BMI (kg/m ²)	27.1 $\pm$ 5.6	14.0	44.7
Haemoglobin (g/dl)			
Male	11.7 $\pm$ 2.2	7.4	16.5
Female	10.0 $\pm$ 1.8	4.2	14.2
Total	11.3 $\pm$ 2.1	4.2	16.5
Preoperative serum creatinine (μ mol/L)	74.5 $\pm$ 30.9	19.0	346.0
Preoperative serum albumin (mg/dl)	32.6 $\pm$ 7.0	8.0	62.0
Characteristic		Frequency (n)	Percentage (%)
Gender	Male	179	57.6
	Female	132	42.4
Anaemia	Male (< 13 g/dl)	96/179	53.6
	Female (< 12 g/dl)	64/132	48.5
	Total	160/311	51.4
Preoperative PRBC transfusion	Given	51	16.4
	Not given	260	83.6
ASA	I	14	4.5
	II	156	50.2
	III	132	42.4
	IV	8	2.6
	V	1	0.3
IHD	Present	30	9.6
	Absent	281	90.4
Heart failure	Present	9	2.9
	Absent	302	97.1
Cerebrovascular disease	Present	10	3.2
	Absent	301	96.8
Stage at surgery	Stage I	54	17.4
	Stage II	83	26.7
	Stage III	110	35.4
	Stage IV	64	20.6
	Right side of colon	92	29.6
Tumour site	Cecum	40	12.9
	Ascending colon	31	10.0
	Hepatic flexure	7	2.3
	Transverse colon	14	4.5
	Left side of colon	97	31.2
	Splenic flexure	5	1.6
	Descending colon	24	7.7
	Sigmoid	68	21.9
	Rectal involvement	122	39.2
	Rectosigmoid	41	13.2
	Rectum	81	26.0

Table 2. Surgical characteristics of patients undergoing surgery for colorectal cancer (N = 311)

Characteristic		Mean $\pm$ S.D	Range
Duration of surgery (min)		337 $\pm$ 151	108–863
Characteristic		Frequency (n)	Percentage (%)
Emergency surgery	Present	70	22.5
	Absent	241	77.5
Type of surgery	Sigmoid resection	69	22.2
	Right hemicolectomy	70	22.5
	Low anterior resection	84	27.0
	Abdominoperineal resection	31	10.0
	Others	57	18.3
Surgical approach	Laparoscopic	127	40.8
	Open	184	59.2
Chemotherapy	Given	182	58.5
	Not given	129	41.5
Preoperative chemotherapy	Given	54	17.4
	Not given	257	82.6
Radiotherapy (n = 122)	Given	76	62.3
	Not given	46	37.7

Table 3. Comparison of surgical outcomes in patients with and without anaemia undergoing surgery for colorectal cancer (N = 311)

Outcome		Anaemia		p-value
		Present (n = 160) Median (IQR)	Absent (n = 151) Median (IQR)	
Duration of surgery (min)		292 (181)	325 (251)	0.140 †
Perioperative blood loss (ml)		300 (350)	300 (350)	0.494 †
Postoperative stay (days)		10 (13)	8 (8)	0.143 †
Duration of monitored care (days)		0 (2)	0 (1)	0.054 †
Outcome		n (%)	n (%)	p-value
30-day stroke	Present	1 (0.6)	1 (0.7)	0.967 β
	Absent	159 (99.4)	150 (99.3)	
30-day mortality	Present	7 (4.4)	4 (2.6)	0.410 α
	Absent	153 (95.6)	147 (97.4)	
Anastomotic leak	Present	18 (13.8)	14 (12.0)	0.660 α
	Absent	112 (85.2)	103 (88.0)	
Postoperative complications	Present	54 (33.8)	30 (19.9)	0.006 α^*
	Absent	106 (66.3)	121 (80.1)	
Troponaemia	Present	28 (17.5)	14 (9.3)	0.034 α^*
	Absent	132 (82.5)	137 (90.7)	
Urine culture	Positive	34 (21.3)	21 (13.9)	0.090 α
	Negative	126 (78.8)	130 (86.1)	
DVT	Present	2 (1.3)	1 (0.7)	0.596 β
	Absent	158 (98.8)	150 (99.3)	
Pulmonary embolism	Present	5 (3.1)	3 (2.0)	0.526 β
	Absent	155 (96.9)	148 (98.0)	
Blood culture	Positive	12 (7.5)	4 (2.6)	0.053 α
	Negative	148 (92.5)	147 (97.4)	
ER visit in first year	Present	73 (45.6)	63 (41.7)	0.488 α
	Absent	87 (54.4)	88 (58.3)	
Recurrence	Present	21 (13.1)	15 (9.9)	0.379 α
	Absent	139 (86.9)	136 (90.1)	

 α Chi-square test was applied. β Fisher's exact test was applied where cell count in one or more cells was less than 5.

† Mann–Whitney U test was applied for non-normally distributed variables.

* p-value ≤ 0.05 was considered statistically significant.

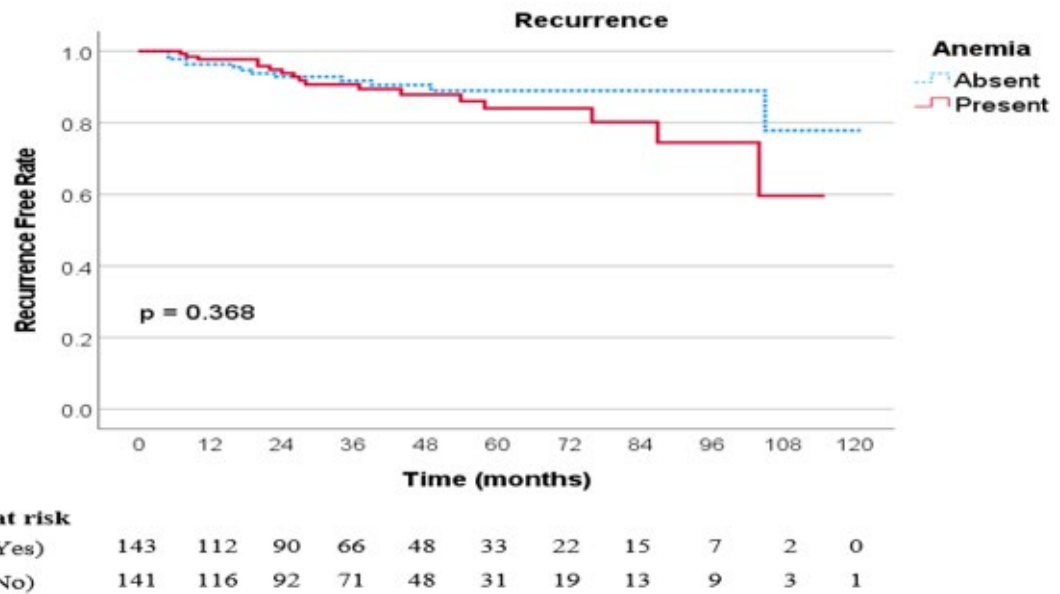


Figure 1. Kaplan–Meier curve showing the effect of anaemia on recurrence in patients operated on for colorectal carcinoma

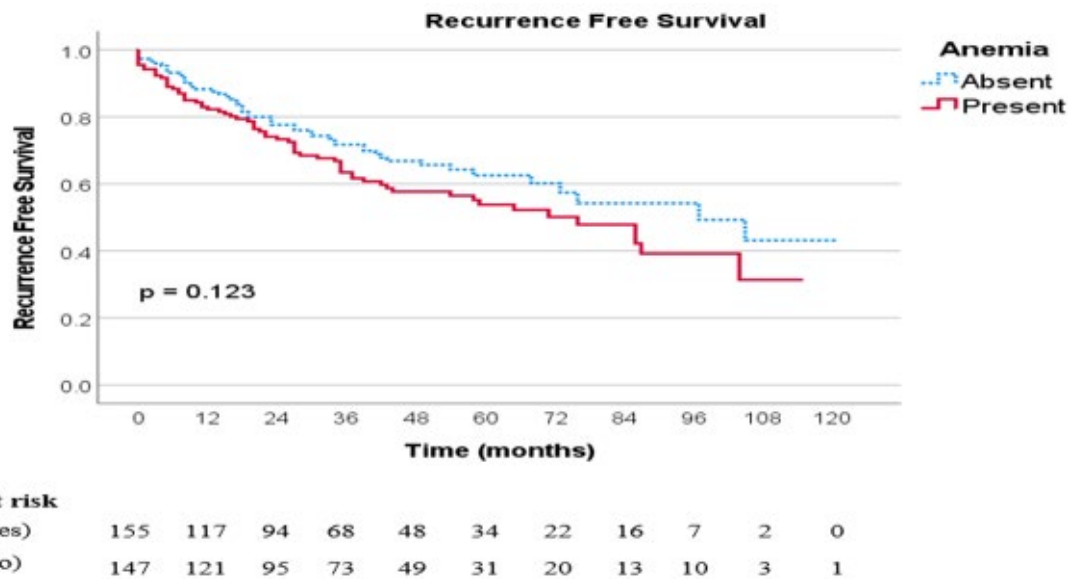


Figure 2. Kaplan–Meier curve showing the effect of anaemia on recurrence-free survival in patients operated on for colorectal carcinoma

Table 5. Cox proportional hazards regression model showing the association of predictors with recurrence

Predictor	Hazard ratio (HR)	95% CI for HR		p-value
		Lower	Upper	
Age $\geq$ 60 years	1.720	0.797	3.708	0.167
Gender (female)	0.938	0.439	2.004	0.869
Anaemia	0.952	0.421	2.152	0.906
Emergency surgery	2.662	1.042	6.800	0.041*
Rectal involvement	2.384	1.049	5.420	0.038*
Perioperative PRBC transfusion	2.540	1.032	6.249	0.042*
Tumour stage III or IV	2.632	1.095	6.327	0.031*

Model fit information:

Likelihood ratio 275.148, $p = 0.002$; * $p \leq 0.05$ was considered statistically significant.

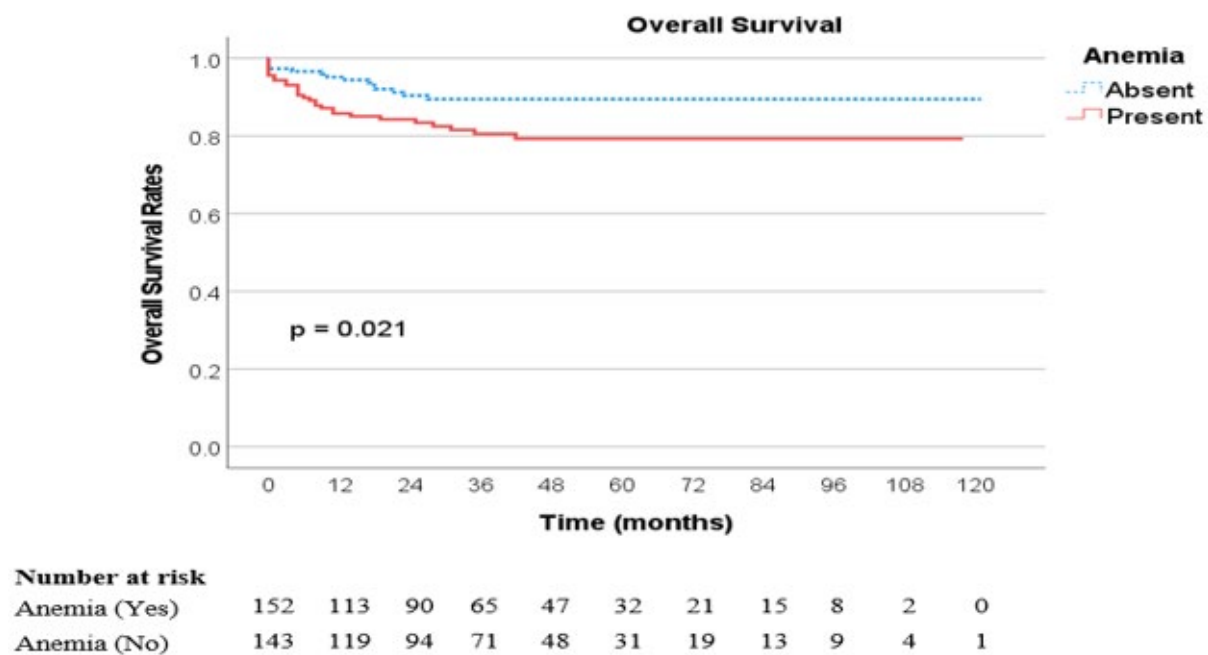


Figure 3. Kaplan–Meier curve showing the effect of anaemia on overall survival in patients operated on for colorectal carcinoma

Table 6. Cox proportional hazards regression model showing the association of predictors with poor outcome (recurrence or mortality)

Predictor	Hazard ratio (HR)	95% CI for HR		p-value
		Lower	Upper	
Age $\geq$ 60 years	2.082	1.425	3.043	< 0.001*
Gender (female)	1.082	0.739	1.584	0.685
Anaemia	1.023	0.682	1.537	0.911
Emergency surgery	2.062	1.336	3.182	0.001*
Rectal involvement	1.018	0.669	1.549	0.935
Perioperative PRBC transfusion	1.926	1.250	2.967	0.003*
Tumour stage III or IV	3.236	2.049	5.110	< 0.001*

Model fit information:

Likelihood ratio 1136.115, $p < 0.001$; * $p \leq 0.05$ was considered statistically significant.

Table 7. Cox proportional hazards regression model showing the association of predictors with mortality

Predictor	Hazard ratio (HR)	95% CI for HR		p-value
		Lower	Upper	
Age $\geq$ 60 years	1.372	0.738	2.551	0.317
Gender (female)	1.175	0.636	2.171	0.606
Anaemia	1.236	0.615	2.484	0.552
Emergency surgery	3.745	1.933	7.255	< 0.001*
Rectal involvement	0.862	0.405	1.835	0.701
Perioperative PRBC transfusion	3.795	1.630	8.832	0.002*
Tumour stage III or IV	2.115	1.019	4.390	0.044*

Model fit information:

Likelihood ratio 429.071, $p < 0.001$; * $p \leq 0.05$ was considered statistically significant.

anaemia on recurrence, recurrence-free survival, and overall survival in patients undergoing surgery for CRC.

The Cox proportional hazards regression analysis showed that emergency surgery (HR: 2.662, CI: 1.042–6.800, $p = 0.041$), rectal involvement (HR: 2.384, CI: 1.049–5.420, $p = 0.038$), perioperative PRBC transfusion (HR: 2.540, CI: 1.032–6.249, $p = 0.042$), and tumour stage 3 or 4 (HR: 2.632, CI: 1.095–6.327, $p = 0.031$)

significantly predicted recurrence. Mortality was significantly predicted by emergency surgery (HR: 3.745, CI: 1.933–7.255, $p < 0.001$), perioperative PRBC transfusion (HR: 3.795, CI: 1.630–8.832, $p = 0.002$), and tumour stage 3 or 4 (HR: 2.115, CI: 1.019–4.390, $p = 0.044$). Tables 5, 6, and 7 summarise the Cox proportional hazards regression models for prediction of recurrence, poor outcome, and mortality (Tables 5, 6 & 7).

DISCUSSION

The prevalence of preoperative anaemia was 51.4% in this cohort of patients with CRC undergoing surgery, which aligns with previously reported rates; a systematic review and meta-analysis found that the prevalence of preoperative anaemia in patients with CRC ranged between 30% and 67%⁸ and was most commonly due to iron deficiency⁷. The high prevalence observed in this cohort is therefore consistent with the literature and likely reflects multifactorial mechanisms – including chronic tumour-related blood loss, nutritional deficiencies, and systemic inflammation⁷.

The current study found that preoperative anaemia was significantly associated with increased short-term postoperative complications, including higher rates of overall morbidity (33.8% vs 19.9%, $p = 0.006$) and postoperative myocardial infarction (17.5% vs 9.3%, $p = 0.034$). This potentially reflects the impact of anaemia on patient physiological reserve and perioperative tolerance; however, findings are not universally consistent. One study of 1,857 patients undergoing surgery for CRC found that although 31.0% were anaemic preoperatively, anaemia was not independently associated with postoperative complications or 30-day mortality. These differences in study findings may be attributable to variations in cancer staging, treatment strategies, patient populations, and how anaemia was defined or stratified⁴.

While preoperative anaemia was not found to have a statistically significant association with cancer recurrence in this cohort, the analysis indicates that it may be a prognostic factor for decreased survival in patients with CRC. This aligns with previous studies (including a meta-analysis and multiple cohort reports) identifying preoperative anaemia as an adverse prognostic factor in CRC^{8,12}.

When analysing colon and rectal cancer studies separately, the negative association of anaemia with OS and DFS largely persisted, with stronger effects observed in rectal cancer [10]. Cohort studies have also reported that anaemia, particularly iron deficiency anaemia, is associated with higher local recurrence; however, the effect on distant metastasis and postoperative complications was less consistent^{12,13}. This association is thought to reflect chronic tumour-related blood loss and nutritional deficiencies which can impair immune function and recovery, particularly in less advanced colon cancers¹². Overall, these findings suggest that anaemia may serve as a marker of poor prognosis in CRC.

The variation in findings across studies highlights that anaemia alone is not a reliable predictor of long-term recurrence or survival, particularly when other risk factors such as tumour stage, emergency surgery, and transfusion history are considered. Recent research has also shown that the aetiology of anaemia is an important predictor of survival. In one retrospective cohort, iron deficiency anaemia and anaemia of inflammation (associated with elevated C-reactive protein levels) were associated with an improved 1-year survival compared with other anaemia types, underscoring the complex interplay between anaemia, inflammation, and cancer outcomes⁷.

The association between anaemia and postoperative complications in the current study underscores the need for early preoperative screening and intervention. With over half of the included patients presenting with anaemia, a simple protocol assessing haemoglobin and iron status could guide appropriate management. Systematic reviews have highlighted that identifying the underlying cause of anaemia – iron deficiency versus inflammation – is crucial, as it influences survival outcomes^{7,15}. Both oral and IV preoperative iron supplementation have been evaluated in patients with CRC. Oral iron offers ease of

administration and lower cost but may be limited by gastrointestinal side effects and a slower haemoglobin response; IV iron provides rapid correction of the deficiency and is shown to reduce postoperative anaemia and complications^{6,16,17,18}. While transfusion remains necessary in some cases, these data, supported by previous evidence^{13,19}, indicate that perioperative transfusions are associated with higher risks of recurrence, mortality, infection, and longer hospitalisation. Therefore, a conservative transfusion approach should be adopted whenever possible, with indications including haemoglobin levels $< 7\text{--}8$ g/dL, history of ischaemic heart disease, or major surgeries such as rectal procedures.

Although not directly measured in this cohort, postoperative anaemia is common (with prevalence estimates ranging from 50.0–90.0%) and negatively affects long-term recovery and quality of life²⁰. Continued management of anaemia after surgery may improve outcomes, especially in patients discharged with low haemoglobin levels.

CONCLUSION

This study has several limitations. First, its retrospective design may have introduced inherent bias and limited causal inferences. Second, single preoperative haemoglobin values, rather than longitudinal measurements, were utilized; this may not reflect patient anaemia status over time. Third, it was not possible to differentiate between anaemia subtypes (such as iron deficiency vs anaemia of chronic disease or autoimmune causes) as most patients lacked available CRP levels and detailed iron studies. Fourth, postoperative haemoglobin was not tracked. Fifth, data on iron supplementation were not collected perioperatively as this could possibly have changed the outcomes. Finally, follow-up was suboptimal, with many patients undergoing surveillance at other centres, potentially impacting the completeness and accuracy of long-term outcomes.

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Competing Interest: None

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