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The Influence of Anaemia and Perioperative Blood Transfusion in The Outcomes of Gastric Cancer

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Anaemia; Gastric cancer; Transfusion; Gastrectomy

1. Abstract

1.1. Background: Gastric cancer is often associated with anaemia, at the time of diagnosis, which may contribute to worse outcomes after surgery. This study aims to evaluate the impact of preoperative anaemia and the need of perioperative transfusions in surgical and oncological outcomes among patients undergoing gastric cancer surgery.

1.2. Methods: This single centre study retrospectively analyses 195 consecutive patients with gastric cancer who underwent curative intent gastric resection, between January 2017 and June 2021. Pre-operative anaemia was defined as Hb<12mg/dL in women and Hb<13mg/dL in men and perioperative blood transfusion was defined as any transfusion within 7 days pre-operatively, during surgery, or during the postoperative hospitalization period. Patient and tumour characteristics, surgical and oncological outcomes were compared (length of stay, complications and survival).

1.3. Results: A total of 195 consecutive patients were included in the study. Anaemia was present in 45.1% of patients, was normocytic in 69.3% and 26.6% received perioperative transfusions. The patients of the anaemic group presented higher age, ASA stage and T and N stages. This group also presented higher perioperatively rates of packed red blood cells (pRBC) transfusion ($p<0.01$) and had longer length of stay ($p=0.01$). The group of transfused patients had higher age ($p=0.03$), higher T ($p<0.001$) and N ($p=0.04$) stages, larger tumour size ($p<0.001$), lower pre-operatory Hb ($p<0.01$) and haematocrit ($p<0.01$), and longer hospital length of stay ($p<0.01$). Cumulative survival curves were significantly different according to anaemia status ($p=0.004$) and the need for transfusion $p<0.001$). The need for blood transfusion was identified as a negative prognostic factor for the outcome of gastric cancer (HR 0.43; 95% CI 0.23-0.80) ($p=0.008$).

1.4. Conclusions: This study suggests that anaemia and perioperative blood transfusions influence the survival of patients with gastric cancer. As blood transfusion emerges as an independent prognostic factor, it is crucial to design a rational approach to control anaemia in patients undergoing gastrectomy.

2. Introduction

Gastric cancer is one of the most common cancers and important cause of cancer-related mortality with an incidence of 136 038 cases and 96 997 deaths in Europe, in 2020 [1]. Preoperative anaemia is commonly found in gastrointestinal (GI) disease and it has been previously thought that, in the gastric cancer population, anaemia was mainly microcytic, due to iron deficit, caused either by chronic occult GI blood loss or deficient oral intake [2]. However, a recent study reported that normocytic anaemia is the most common type of anaemia in patients with GI cancer [3,4]. Thus, the cause of pre-operative anaemia in GI cancer patients remains uncertain and it might be probably multifactorial with an association of nutritional deficiencies, chronic blood loss, oncologic treatment and a chronic inflammatory state.

Anaemia is frequently associated with worst surgical outcomes, such as longer length of stay, presence of complications and poorer overall survival. It is also a strong indicator for the need of packed red blood cells (pRBC) transfusion, which is neither harmless nor free from complications [4,5]. Although transfusion has been associated with adverse effects, increase of morbidity and mortality, in what concerns gastric cancer, the impact of transfusions on post-operato-

ry outcomes remains controversial. Indeed, some recent studies seem to establish an association between transfusions and poorer surgical outcomes and survival, but the results are far from being universally observed [6-9]. Preoperative anaemia, either by itself or by the need of associated pRBC, is believed to be a marker of worst systemic status, therefore its prompt identification and subsequent preoperative correction is advisable, mainly in the set of elective surgical resection. The main purpose of this study was to evaluate the impact of preoperative anaemia and perioperative pRBC transfusion in outcomes of patients with gastric cancer, undergone curative intent surgery. Outcomes evaluated were length of stay, complications and overall survival.

3. Material and Methods

3.1. Study Design

The present study retrospectively evaluated a series of 195 consecutive patients with proved gastric cancer by biopsy who underwent curative intent gastric resection, in the Department of General Surgery of CHTMAD (Centro Hospitalar de Trás-os-Montes e Alto Douro), between January 2017 and June 2021. All the 436 patients who were diagnosed with gastric cancer by biopsy were identified, and the patients who underwent gastric resection surgery were included in this study. Patients with metastatic disease at time of diagnosis, patients that underwent palliative intervention as first line treatment and patients in whom surgical resection was not possible, were excluded.

3.2. Parameters Evaluated

Demographics, clinical information, pathological variables including laboratory results, staging according to the 8th edition of the TNM Classification of Malignant Tumours by Union for International Cancer Control (UICC), tumour size, lymph node dissection type, type of surgery as well as data on treatment outcomes were collected to build a database. Patients were categorized by the presence of anaemia according to the World Health Organisation guideline (males: haemoglobin <13mg/L and female: haemoglobin <12mg/L) [9]. According to the need of blood transfusion, cases were categorized into "yes" and "no", and when applicable, the number of blood units was identified. The cut-off for transfusion was bellow 7g/dL and 8g/dL, through the presence of ischemic cardiopathy or not, respectively [10]. Patients were submitted to distal gastrectomy or to total gastrectomy depending on the location of the tumour (distal cancers and proximal cancers, respectively) or the histotype - according to Lauren classification. Cases with less than 25 nodes retrieved were classified as D1 lymphadenectomy, and as D2 if at least 25 lymph nodes were retrieved. In brief, regarding the depth of gastric wall invasion, cases were classified into pT1 (invasion limited to the submucosa layer), pT2 (those invading the muscular layer), pT3 (those invading the subserosa layer), and pT4 (those spreading to the serosa layer neighbouring organs). Regarding the nodal status, cases were classified into pN0 (no lymph nodes with metastases), pN1 (1-2 invaded lymph nodes), pN2 (3-6 lymph nodes) and pN3 (>6 lymph nodes). To facilitate statistical analysis, cases were also classified as positive and negative according to nodal status.

Post-operative complications were classified using the Clavien-Dindo score [11].

3.3. Statistical Analysis

SPSS 25 (SPSS, Inc., Chicago, IL) computer program was employed in the statistical analysis of data. Distributions of cases was compared by χ^2 test. Cumulative survival curves were obtained by the Kaplan- Meier method [12] and compared through the log rank test. Cox regression stepwise approach (proportional hazard model) was used to identify the prognostic factors. Cumulative overall survival was defined as the period between date of surgery and date of death by any cause or date of censoring (October 01, 2021). Significance was assumed if p values were less than 0.05.

4. Results

4.1. General Data of Patients

A total of 436 patients were diagnosed with gastric cancer, documented on biopsy specimens, over a period of 3.5 years – January of 2017 to June of 2021. Of these, 195 patients (118 males and 77 females, and median age of 70 years old) underwent gastric resection surgery and thus were included in this study. Patients submitted to surgery but without resection or even not candidates for surgery were excluded (n=241). Forty-five patients (23%) underwent neoadjuvant chemotherapy followed by surgery and 149 (77%) primary resection surgery. The predominant type of surgery was distal gastrectomy (62.2%, n=122) and the predominant approach was laparotomy (88.7%, n=173).

4.2. Presence of Anaemia and its Association with Patient Characteristics and Outcomes

In the study, 45% (n=88) of patients presented anaemia, which was normocytic in a major percentage (69%, n=60).

Table 1 summarizes the distribution of cases according to several clinical and pathological characteristics and the presence of anaemia. The distribution of cases identified significant differences between anaemia and no-anaemia according to the following parameters: age and ASA score of the patients; depth of wall penetration, nodal status, and tumour size. The age of patients with anaemia was higher compared to that of those without anaemia (Mdn (IQR) 74 (65-78) vs 67 (60-76) years-old, p=0.034). The percentage of anaemic patients catalogued into higher classes of ASA score was higher compared to that of patients without anaemia catalogued into the same classes of ASA (60.2% vs 43.0%, p<0.001). The percentage of larger tumours in patients with anaemia was higher than in non-anaemia group (52.3% vs 17.5%, p<0.001). The relative frequency of cases with more advanced wall depth penetration, i.e. pT3-4, by the tumour, was higher in the anaemic group than that observed in the non-anaemia group (62.5% vs 30.1%) (p<0.001) and the percentage of patients with lymph node metastasis (N+) was higher in the anaemic group (53.4% vs 31.1%, p=0.02). No significant differences were observed in the distribution of the other evaluated parameters.

Table 1: Characteristics of population based on presence of anaemia. ASA, American Society of Anesthesiology; GEJ, Gastroesophageal junction; IQR – Interquartile range; Mdn - Median; Pos – Positive; Neg – Negative.

Table 1	Anemia (n=88)	Non-anaemia (n=107)	*p* value
Male sex, % (n)	55.7 (49)	64.5 (69)	0.135
Age – Mdn [IQR]	74 [65-78]	67 [60-76]	**0.034**
ASA score, % (n)			**<0.001**
I+II	39.8 (35)	57.0 (61)	
≥III	60.2 (53)	43.0 (46)	
Tumor extension, % (n)			**<0.001**
pT1- pT2	37.5 (33)	69.9 (72)	
pT3 - pT4	62.5 (55)	30.1 (31)	
Node Status, % (n)			**0.021**
N-	46.6 (41)	68.9 (73)	
N+	53.4 (47)	31.1 (33)	
Type of cancer*% (n)			0.930
Intestinal	70.5 (62)	69.2 (74)	
Diffuse	15.9 (14)	21.5(23)	
Unclassified	13.6 (12)	9.3 (10)	
Tumour size			**<0.001**
< 2 cm	9.3 (8)	37.9 (39)	
2-5 cm	38.4 (33)	44.7 (46)	
>5 cm	52.3 (45)	17.5 (18)	
Neoadjuvant therapy, % (n)	25.0 (22)	20.6 (22)	0.461
Tumor site, % (n)			0.339
GEJ	8.0 (7)	4.7 (5)	
Gastric	92.0 (81)	95.3 (102)	
c-erb-B2, % (n)			0.257
Pos	8.6 (5)	5.3 (2)	
Neg	91.4 (53)	94.7 (36)	

4.3. Relationship Between Anaemia, Blood Transfusion, and Overall Survival

In this series, 48 patients (24.6%) were submitted to blood transfusion. Table 2 summarizes the distribution of cases according to the several parameters evaluated (perioperatory transfusion, units of pRBC, complications and length of stay) and the presence of anaemia. Anaemia was associated with a significantly higher rate of transfusion at any time (perioperatively – 44.3% vs 8.4%, p<0.001), and higher pre-operative (23.9% vs 0.9%, p<0.001), intra-operative (12.5% vs 2.8%, p=0.009) and pos-operative (18.2% vs 6.5%, p=0.014) transfusion rate. The length of stay was also significantly higher in the anaemic group (Mdn (IQR) 10 (8-13) days vs 9 (8-11) days, p= 0.01). The median pRBC transfusion was identical between groups and there were no significant differences between rate or severity of complications. Anaemia was significantly associated (p = 0.004) with poorer overall survival (Fig. 1A), however it was not an independent prognostic factor in Cox multivariate analysis (p>0.05).

Table 2: Outcomes of patients with and without anaemia. IQR – Interquartile range; Mdn - Median; Pos – Positive; Neg – Negative; pRBC - packed red blood cell transfusion.

Table 2	Anaemia (n=88)	Non-anaemia (n=107)	*p* value
Perioperatory Transfusion, % (n)			**<0.001**
Yes	44.30 (39)	8.40 (9)	
No	55.70 (49)	91.60 (98)	
Pre-operatory, % (n)			**<0.001**
Yes	23.9 (21)	0.9 (1)	
No	76.1 (67)	99.1(106)	
Intra-operatory, % (n)			**0.009**

Yes	12,5 (11)	2.8 (3)	
No	87.5 (77)	97.2 (104)	
Post-operatory, % (n)			**0.014**
Yes	18.2 (16)	6.5 (7)	
No	81.8 (72)	93.5 (100)	
pRBC (Mdn)	2 [1 - 3]	2 [1 - 3]	-
Complication, % (n)			
Any	36.8 (32)	29.9 (32)	0.195
Minor	37.5 (33)	43.8 (47)	0.799
Major - CD >III	62.5 (55)	56.3 (60)	
Length of stay (days), Mdn [IQR]	10 [8-13]	9 [8-11]	**0.017**

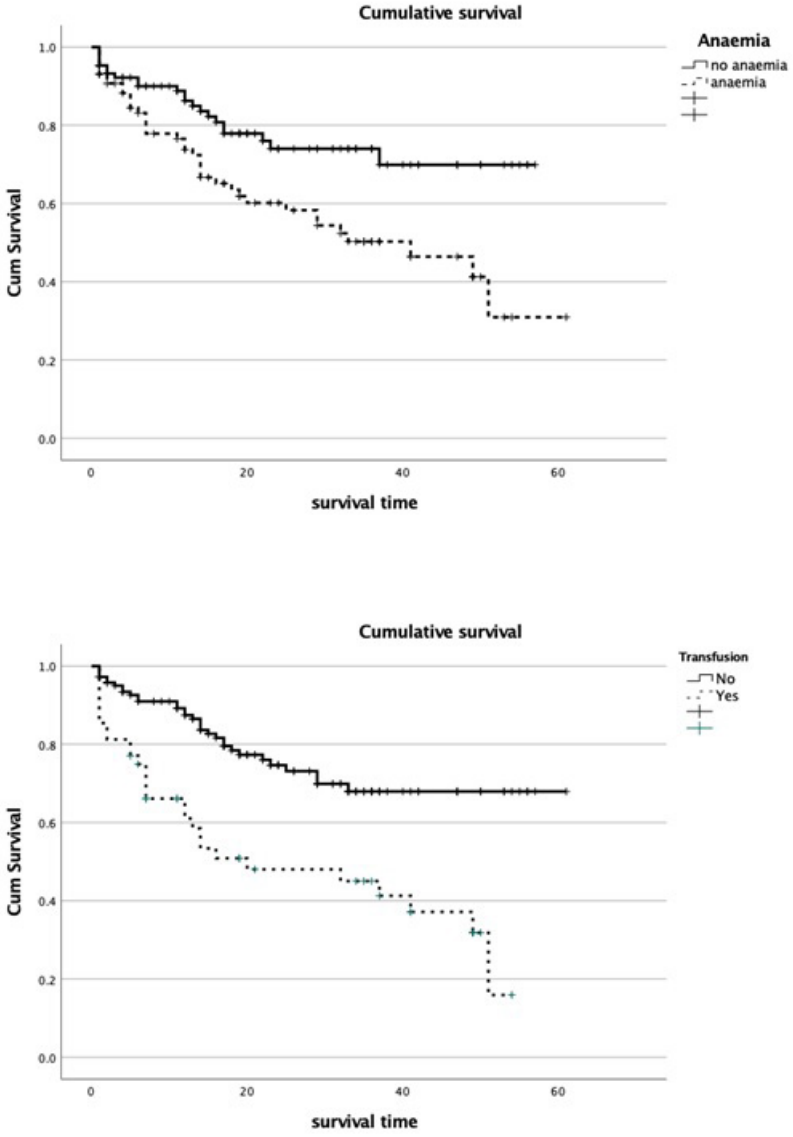

Figure 1: Kaplan Meier curves of overall survival in patients who underwent gastric resection surgery grouped according to A presence of anaemia (p = 0.004), and B need of transfusion (p<0.001).

4.4. Relationship Between Blood Transfusion and the Characteristics of Both Patients and Tumours

Table 3 summarizes the distribution of cases according to the several parameters evaluated and the need for blood transfusion. By comparing patients between the two groups according to the need for transfusion, this study identified that the transfused patients presented higher age (Mdn (IQR) – 74 (65-78) vs 67(60-76) years-old, p=0.03), larger tumour size (tumour >5cm in transfused: 55.3% vs in no transfused: 26.1%, p<0.001) and higher T (T3-T4 in transfused: 66.7% vs in no transfused: 36.7%, p<0.001) and N stages (N+ in transfused: 58.3% vs in no transfused: 35.4%, p=0.04). Transfused patients also had more complications (50% vs 27%, p=0.04), longer hospital length of stay (Mdn (IQR) - 14.5 (9-24.5) vs 9 (8-10) days; p<0.01), and lower pre-operative haematocrit (Mdn (IQR)– 31 (28-37) % vs 39 (35-43) %; p<0.01) and Hb level (Mdn (IQR) 9.75 (8.5-11.7)g/dL vs 13 (11.5-14.3)g/dL; p<0.01). There was not a statistically significant difference in ASA score between the two groups. Blood loss during surgery had similar median values between groups and there were no differences in the type of surgical approach (open vs minimally invasive).

Table 3: Outcomes of patients with and without transfused packed red cells. ASA, American Society of Anesthesiology; GEJ, Gastroesophageal junction; Hb – Haemoglobin; IQR – Interquartile range; Mdn – Median.

	Transfusion (n=88)	No Transfusion (n=147)	*p* value
Age – Mdn [IQR]	74[65-78]	67[60-76]	**0.030**
ASA score, % (n)			0.246
I	0	1.4 (2)	
II	39.6 (19)	51 (75)	
≥III	60.4 (29)	47.6 (70)	
Tumour size*			**<0.001**
< 2 cm	8.5 (4)	30.3 (43)	
2-5 cm	36.2 (17)	43.7 (62)	
>5 cm	55.3 (26)	26.0 (37)	
pT (TNM) (n)			**<0.001**
T1-T2	33.3 (16)	63.3 (93)	
T3-T4	66.7 (32)	36.7 (54)	
Node Status, % (n)			**0.04**
N-	41.7 (20)	64.6 (95)	
N+	58.3 (28)	35.4 (52)	
Type of surgery % (n)			0.416
Laparotomy	93.8 (45)	87.1 (128)	
Laparoscopy	4.2 (2)	10.2 (15)	
Conversion	2.0 (1)	2.7 (4)	
Type of lymph node dissection			0.404
D1 (<=25)	85.4 (41)	78.9 (116)	
D2 (>25)	14.6 (7)	21.1 (31)	
Type of gastrectomy			0.308
Subtotal	56.3 (27)	64.6 (95)	
Total	43.8 (21)	35.4 (52)	
Blood loss (mL) – Mdn	100	100	-
Complications			
Any	50 (24)	27,4 (40)	**0.040**
Minor	33,3 (8)	45 (18)	**0.050**
Major - CD >III	66,7 (16)	55 (22)	
Length of stay (days), Mdn [IQR]	14.5 [9-24.5]	9 [8-10]	**<0,01**
Htc (%) Mdn – Mdn [IQR]	31 [28-37]	39 [35-43]	**<0.01**
Pre-operative Hb (g/dL) – Mdn [IQR]	9.75 [8.5-11.7]	13 [11.5-14.3]	**<0.01**

* Only 189 from 195 patients had data about tumour size.

4.5. Cumulative Survival and Outcome in Gastric Cancer Cases According to the Presence of Anaemia and the Need for Transfusion

Figure 1 illustrates the cumulative survival curves for groups of patients according to the presence of anaemia (Figure 1A) and the need for blood cell transfusion (Figure 1B). After a median follow up of 20 months, 61 patients (31.3%) had died from all causes. Five-year survival rate for patients without anaemia (69.9%) was higher than that observed in anaemic patients (52.4%). Cumulative survival curves according to the presence or absence of anaemia, revealed worse survival in the anaemic group (p=0.004). Survival rate at median 20 months of follow-up for patients submitted to blood transfusion (15.9%) was lower than that the 5-year survival rate observed in patients who did not need transfusion (67.9%). The cumulative survival curves according to transfusion need, revealed worse survival in the transfused group(p<0.001). Table 4 summarizes the results of Cox regression model to evaluate prognostic factors of gastric cancer cases. In this model, multiple variables were evaluated, namely tumour characteristics (status T, status N), type of surgery (open vs laparoscopic), sex, presence of anaemia, presence of complications and pRBC transfusion, but only the variables with statistically significant results were presented in table 4. In the evaluated series, the presence of anaemia did not emerge as an independent prognostic factor. Indeed, the multivariate model identified only nodal status (p<0.001), perioperative complications (p=0.006) and blood transfusion (p=0.008) as the independent prognostic factors. According to the model, the prognosis was poorer whenever blood transfusion was needed (HR 0.43: 95% CI 0.23-0.80).

Table 4: Multivariate Cox regression (stepwise) analysis for gastric carcinomas. (*) Indicator parameter, pN3b; (**) Indicator parameter, the presence of complications; (***) Indicator parameter, the need for blood transfusion.

			95% CI for HR	
Parameter	*p* value	HR	Lower	Upper
pN(*)	**<0.001**			
pN0	**<0.001**	0.08	0.02	0.24
pN1	**0.012**	0.26	0.09	0.75
pN2	**0.051**	0.34	0.11	1.04
pN3a	**0.017**	0.22	0.07	0.76
Complications (**)	**0.006**	0.43	0.23	0.79
Transfusion (***)	**0.008**	0.43	0.23	0.80

5. Discussion

Anaemia is a common finding among patients with gastric cancer and is usually associated with the need for transfusion [13]. This study reported 45% of anaemic patients, most of them had normocytic anaemia (69%), rather than the anticipated microcytic anaemia classically associated with GI cancers. This findings agree with results reported by Benson Yl Chan et al [5]. A small fraction of patients with microcytic anaemia in this study, suggests that pre-operative anaemia is probably multifactorial and unlikely to be simply caused by chronic occult GI blood loss. Indeed, the host innate systemic inflammatory response to cancer is associated with the observed normocytic anaemia. However, most patients in this study did not have their total body iron storage, ferritin or transferrin saturation levels measured and categorized, hence some patients with normocytic anaemia could have had low iron stores which were unrecognised [5,14,15]. Also, there was no information about previous iron supplementation in all patients, so this variable was not analysed. When comparing the characteristics of patients with and without anaemia, this study reported higher age, ASA stage, T and N stages and larger tumours in the anaemic population, which is not surprising considering anaemia is expected to be more prevalent in older patients and with higher ASA stages, mainly because these patients usually may have other comorbidities. Also, larger tumours and higher T and N stages translate to a more advanced disease, with higher systemic inflammatory status, poorer health status, which was consistent with the reported by other studies [4,5]. As Benson Yl Chan et al, this study also reported a poorer overall survival, longer length of stay and higher transfusion rate in the anaemic group [5]. In this population, cumulative survival was influenced by both anaemia and the need for blood transfusion. Despite anaemia might be dependent on other factors which strongly influence survival, in this concrete population, there are other studies that report anaemia as an independent prognostic factor. Chan et al reported anaemia as an independent factor to overall survival and as leading cause of perioperative pRBC transfusions [5]. Huang's meta-analysis, also reported anaemia as predictor of worst prognosis, affecting overall survival and disease-free survival. The exact mechanism is not yet understood but might be related to systemic inflamation and tumour hypoxia, inducing tumour progression via genetic changes and increasing the resistance to therapy. Furthermore, anaemia has been associated with advanced tumour stages, which influence the prognosis [16]. Perioperative blood transfusions have been described as having detrimental effects on prognosis after gastric cancer surgery [7,8,17]. Such effects may be related to cellular immunity compromise, decreasing delayed-type hypersensitivity, suppressing T-cell proliferation and destroying the functions of natural killer cell. This immunosuppression status increases the risk of postoperative infectious complications and probably favours recurrence of gastric cancer, since it may cause progression and fail to clear disseminated tumour cells in bone marrow and circulation [18]. However, controversy exists regarding the true impact of blood transfusions, since other studies revealed that it has no impact in overall survival [6,19]. According to some studies, pRBC transfusion effects could be det-

rimental coincidental rather than causative. The coincidental factors might be related to tumour (size, depth of invasion, node involvement), patient (age, comorbidity), or surgery (intraoperative complication or difficult dissection) resulting in more blood loss and more transfusions [20]. In this study, anaemic patients needed more transfusions and pRBC transfusion was associated with older age, higher T and N stage and larger tumour size which was coincident with the results of studies [7,17]. Like the results of a study by Kammili et al, this study also reports that transfused patients had longer length of stay and more complications [6]. Transfusion has been reported as having a strong negative impact in survival. Indeed, in multivariate analysis, using Cox regression model, in this series, we identified blood transfusion, as well as nodal status and perioperative complications as the only independent predictors of survival. Therefore, our results are in line with some other studies which seem to indicate that pRBC transfusion does influence the long-term survival of patients with resected gastric adenocarcinoma [21]. Due to the multifactorial nature of anaemia, it is important to recognise and subcategorize it by aetiology, to allow a more effective management before programmed surgery, namely iron therapy institution, while minimizing potentially harmful blood transfusions. Since pRBC transfusions may be associated with worse postoperative short-term outcomes in patients with gastric cancer, blood management strategies like patient blood management protocols, rather than merely blood transfusion, should be implemented, in order to reduce the use of pRBC in the perioperative period [22]. Although this study concerns multiple variables, there are still some limitations. First limitation is the retrospective nature of the study and size of the sample which could bias some analysis results. Second, there was no complete data in patients from years before 2017, so the follow up period can weaken the conclusions of the study. Another limitation was the lack of data on iron status of the patients, which makes it very difficult to distinguish between functional and absolute iron deficiency, particularly in the normocytic anaemia group. Further investigation of iron status in the context of inflammation in these patients might help guide the treatment of anaemia in this group. Therefore, it is necessary to carry out prospective, randomized, controlled studies to investigate the prognostic effect of blood transfusion in patients with gastric cancer. Summing up, according to this study, in patients with gastric cancer undergoing surgical curative treatment, anaemia was associated with higher rates of perioperative blood transfusion, which was an independent key factor to the poor outcome of gastric cancer, thus claiming for a more rational and tailored perioperative approach.

References

1. Sung H. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021; 71(3): 209-249.
2. Thomas DW. Guideline for the laboratory diagnosis of functional iron deficiency. Br J Haematol. 2013; 161(5): 639-48.
3. F Lourenco, EH, S El-Ghazali, G Kokri, R Krishna, S Kadri. PWE-123 Haematological profile of oesophago-gastric cancers at point of diagnosis: a large single centre study. BMJ. 2017.
4. Moral Garcia V. Anemia as a surgical risk factor]. Med Clin (Barc). 2013; 47-54.
5. Chan BY. Impact of anaemia in oesophago-gastric cancer patients undergoing curative treatment by means of neoadjuvant chemotherapy and surgery. Surg Oncol. 2021; 38: 101585.
6. Kammili A. Perioperative Transfusions for Gastroesophageal Cancers: Risk Factors and Short- and Long-Term Outcomes. J Gastrointest Surg. 2021; 25(1): 48-57.
7. Liu X. Effect of perioperative blood transfusion on prognosis of patients with gastric cancer: a retrospective analysis of a single center database. BMC Cancer. 2018; 18(1): 649.
8. Nakanishi K, M Kanda, Y Kodera. Long-lasting discussion: Adverse effects of intraoperative blood loss and allogeneic transfusion on prognosis of patients with gastric cancer. World J Gastroenterol. 2019; 25(22): 2743-2751.
9. WHO Scientific Group on Nutritional Anaemias, W.H.O., Nutritional Anaemias Report of a WHO Scientific Group [meeting Held in Geneva from 13 to 17 March 1967]. World Health Organization Technical Report Series. 1968.
10. Mueller MM. Patient Blood Management: Recommendations From the 2018 Frankfurt Consensus Conference. JAMA. 2019; 321(10): 983-997.
11. Clavien PA. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009; 250(2): 187-96.
12. Kaplan EL, P Meier. Nonparametric estimation from incomplete observations. J Am Stat Assoc. 1958; 53: 457-481.
13. Birgegard G. Cancer-related anemia: pathogenesis, prevalence and treatment. Oncology. 2005; 68: 3-11.
14. Uprichard WO, J Uprichard. Investigating microcytic anaemia. BMJ. 2013; 346: f3154.
15. McSorley ST. Normocytic anaemia is associated with systemic inflammation and poorer survival in patients with colorectal cancer treated with curative intent. Int J Colorectal Dis. 2019; 34(3): 401-408.
16. Huang XZ. Preoperative Anemia or Low Hemoglobin Predicts Poor Prognosis in Gastric Cancer Patients: A Meta-Analysis. Dis Markers. 2019; 7606128.
17. Xu D. Perioperative blood transfusion is one of the factors that affect the prognosis of gastric cancer. J BUON. 2018; 23(3): 672-677.
18. Sun C. Allogeneic blood transfusion and the prognosis of gastric cancer patients: systematic review and meta-analysis. Int J Surg. 2015; 13: 102-110.
19. Xiao H. Peri-Operative Blood Transfusion Does Not Influence Overall and Disease-Free Survival After Radical Gastrectomy for Stage II/III Gastric Cancer: a Propensity Score Matching Analysis. J Gastrointest Surg. 2018; 22(9): 1489-1500.
20. Rausei S. Peri-operative blood transfusion in gastric cancer surgery: prognostic or confounding factor? Int J Surg. 2013; S100-3.

21. Sanchez-Bueno F. Does perioperative blood transfusion influence long-term prognosis of gastric cancer? Dig Dis Sci. 1997; 42(10): 2072-6.

22. Elmi M. The impact of blood transfusion on perioperative outcomes following gastric cancer resection: an analysis of the American College of Surgeons National Surgical Quality Improvement Program database. Can J Surg. 2016; 59(5): 322-9.