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Simplified diagnostic algorithm for classification of preoperative anaemia based on complete blood count and its application in elective gastrointestinal surgery

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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ABSTRACT:

Introduction: Anaemia is associated with increased morbidity, mortality, hospital length of stay, and requirement for blood transfusion. Early differential diagnosis of anaemia may expedite its treatment and improve outcomes in the perioperative setting. The aim of our study was to create a simplified diagnostic algorithm for classification of anaemia based on complete blood count and to test its applicability in an elective gastrointestinal surgical population.

Material and methods: Selected clinical data and laboratory red blood cell parameters were retrieved retrospectively for the group of 442 consecutive patients scheduled for elective high-risk gastrointestinal surgery from January 2016 to August 2018. Based on pathophysiologic data we created a simplified diagnostic algorithm for classification of preoperative anaemia and applied it to the study population.

Results: Using the cut-off value of 130 g L-1 for both sexes, anaemia was diagnosed in 166 patients (37.5%). As many as 29 (17.5%) anaemic patients had aetiology of anaemia accurately established using our simplified diagnostic algorithm – either iron or vitamin B12/folate deficiency.

Discussion: Preoperative anaemia is common in elective gastrointestinal surgery. Simplified diagnostic algorithm based solely on complete blood count parameters is helpful in the preliminary identification of patients with iron and vitamin B12/folic acid deficiencies so haematinic supplementation can be started early in preparation for surgery.

KEYWORDS: algorithms, anaemia, iron-deficiency, preoperative period, surgery

INTRODUCTION

Anaemia is associated with increased morbidity, mortality, hospital length of stay, and requirement for packed red blood cell (PRBC) transfusion. PRBC transfusion is itself associated with increased morbidity and mortality [1]. According to the World Health Organisation (WHO) anaemia is a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiological needs, which vary by age, sex, altitude, smoking and pregnancy status. The WHO defines anaemia as haemoglobin concentration below 120 g L-1 in women and 130 g L-1 in men, although the cut-off value had been chosen arbitrary [2]. According to a recent consensus [3], the target for preoperative haemoglobin concentration should be ≥ 130 g L-1 independent of gender. Taking into account intraoperative blood loss, patients should have their anaemia diagnosed and properly managed well in advance of a planned surgery in order to minimize the risk of transfusion and associated complications. Due to the high prevalence of anaemia in surgical population it is crucial to identify and manage it preoperatively. Complete blood count (CBC) is routinely ordered as a component of the preoperative laboratory panel, whereas iron status markers, like ferritin concentration and transferrin saturation, are not. Early differential diagnosis of anaemia may expedite treatment and improve patients' outcomes in the perioperative setting. The aim of our study was to analyse the incidence of preoperative anaemia in elective gastrointestinal (GI) surgery, create a simplified diagnostic algorithm for classification of anaemia based solely on parameters derived from CBC, and test its applicability in an elective GI surgical population.

MATERIAL AND METHODS

Selected red blood cell (RBC) parameters derived from CBC tests performed in the Central Laboratory of the University Clinical Centre of Medical University of Silesia, Katowice, Poland were reviewed retrospectively for the group of consecutive patients scheduled for elective high-risk GI surgery from January 2016 to August 2018. The surgery was classified as high-risk using European Society of Cardiology/European Society of Anaesthesiology guidelines [4]. CBC tests were performed using a standard laboratory analyser (XT-1000i, Sysmex, United Kingdom), blood was collected in 5-mL EDTA (Ethylenediaminetetraacetic Acid) test tubes. The analysed RBC parameters with reference values are presented in Tab. I.

Based on pathophysiological data we created a simplified diagnostic algorithm for classification of preoperative anaemia (Fig. 1.). We were very careful to create an algorithm that would identify true haematinic deficiency cases, either iron or vitamin B12/folic acid. There was no room for false results as the main intervention in iron deficiency anaemia is iron supplementation, and that could lead to iron intoxication if anaemia was wrongly classified as iron deficiency. Taking this into account we classified anaemia as iron deficiency (IDA) only if we saw two most characteristic features of iron deficiency, namely microcytosis and hypochromia. However, beta-thalassemia and sideroblastic anaemia may present with similar features on a peripheral blood smear and iron supplementation in these patients is contraindicated. In order to rule out these two conditions we included mean corpuscular hae-

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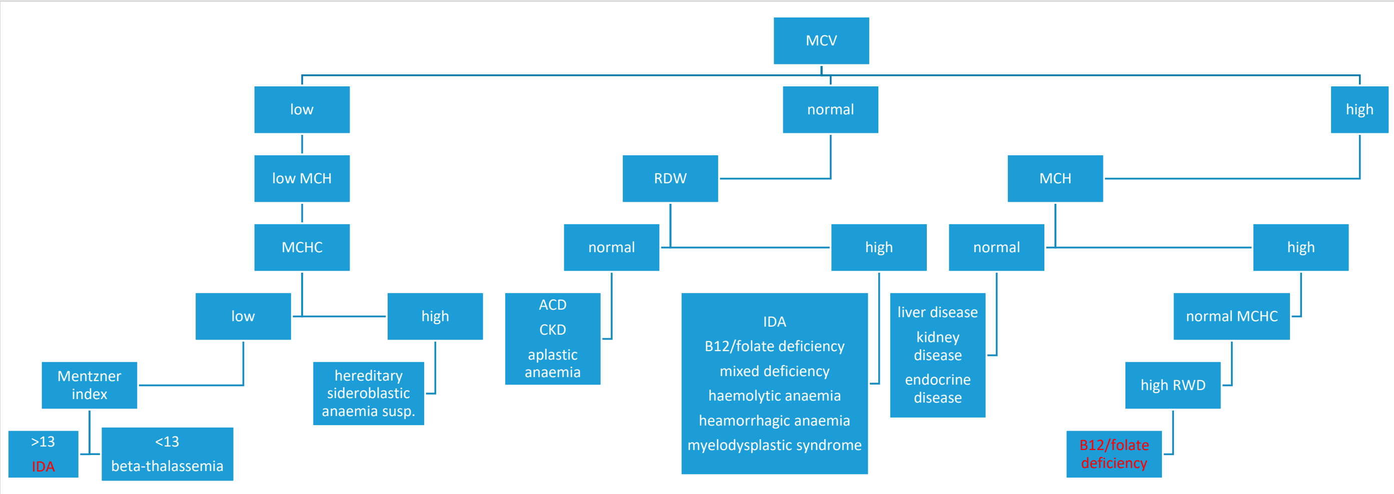

Fig. 1. Simplified diagnostic algorithm for classification of preoperative anaemia.

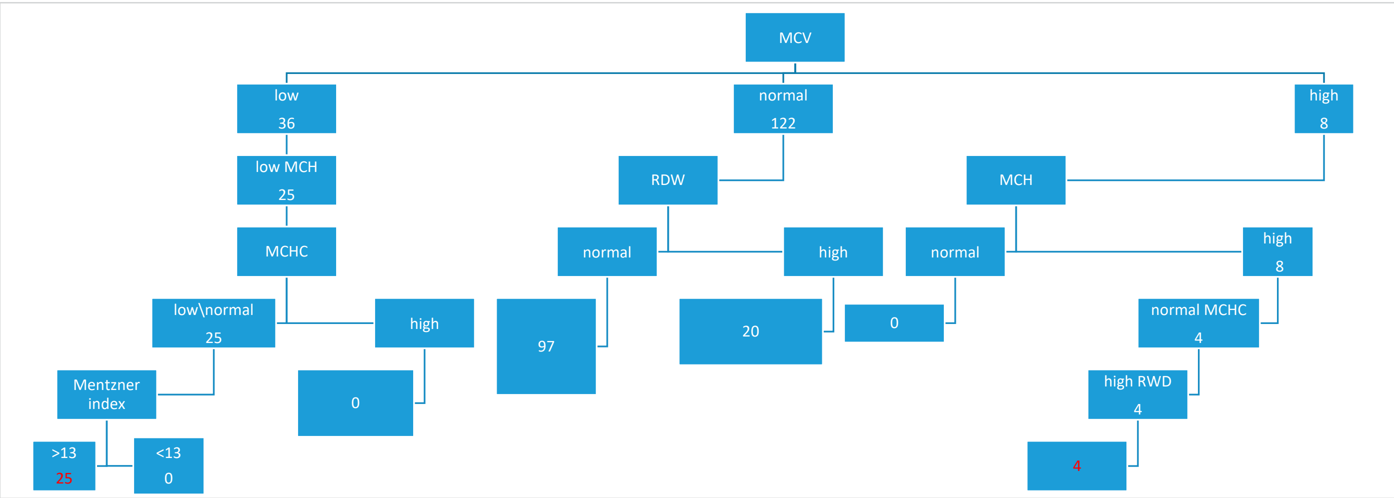

Fig. 2. Classification of preoperative anaemia.

moglobin concentration (MCHC) and Mentzner index [5] in our diagnostic algorithm. Similarly, in case of vitamin B12/folate deficiency, we precisely defined this type of anaemia as megaloblastic – high values of mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) – with normal values of MCHC and high red cell distribution width (RDW).

The first step in diagnosis of preoperative anaemia according to our algorithm is to confirm that haemoglobin concentration is below 130 g L-1 (both sexes). The next step is to check MCV, MCH, MCHC and RDW. Our simplified diagnostic algorithm based on pathophysiologic features was applied to the study population.

RESULTS

The study population consisted of 442 patients. Demographic and clinical data of the studied patients are presented in Tab. II.

Median haemoglobin (g L-1) in men was 137 (IQR 125–148) and in women 133 (IQR 121–139). Using the cut-off value of 130 g L-1 for both sexes, anaemia was diagnosed in 166 patients (37.5%). The incidence of preoperative anaemia was 33.9% in men (77/227) and 40.9% in women (88/215). There were also differences in the prevalence of preoperative anaemia based on age (< 65 and ≥ 65 years) [6]. Overall anaemia was present in 38.8% of patients below 65 years and in 36.7% of patients in the age group of 65 years and above. Anaemia was present in 33.6% (36/107) of younger men and in 35% (42/120) of older men, whereas for women the incidence was 43.3% (52/120) and 37.9% (36/95), respectively.

We applied our simplified diagnostic algorithm for classification of preoperative anaemia to the study population [Fig. 2.]. Working through the algorithm the majority of anaemic patients were diagnosed with normocytic anaemia (122 patients, 73.5%), 36 patients (21.7%) with microcytic and 8 patients (4.8%) with macrocytic anaemia. As many as 29 (17.5%) anaemic patients had aetiology of anaemia accurately established using our simplified diagnostic algorithm – either iron or vitamin B12/folate deficiency. Nevertheless, the majority of anaemic patients in our study had normocytic anaemia (73.5%) and further testing was required to accurately establish the aetiology of preoperative anaemia.

DISCUSSION

Anaemia in preoperative period is common. According to a large study, the estimated prevalence of preoperative anaemia, based on

WHO criteria, was 31.1% in women and 26.5% in men [7]. In our study, the prevalence of anaemia was higher, 37.5%, however, we used a new cut-off value for anaemia diagnosis [3]. This is a more sound approach, as women bleed as much as men during surgery and additionally have lower blood volumes.

According to PolSenior study, anaemia (WHO criteria) was present in 17.4% of population above 65 years old [6]. In our study, the prevalence of anaemia in the senile group was much higher – 36.7%; however, this was based on the new consensus (130 g L-1 for both sexes). It is important to note that the aetiology of anaemia in this particular age group is multifactorial. There are several well-known processes leading to anaemia in old age. First of all, the haematopoietic cells of the bone marrow are progressively replaced by adipocytes and fibroblasts. Secondly, erythropoietin synthesis decreases as a result of reduction of the number of active nephrons [6]. Lastly, the occurrence of anaemia in old age is accelerated by numerous comorbidities.

Anaemia in the preoperative period is a problem on its own as it increases mortality and morbidity, for instance acute kidney injury [8]. It is also a risk factor for allogenic blood transfusion in the perioperative period. Allogenic blood transfusion leads to immunomodulation and decreases recurrence-free survival in cancer patients [9], which may have serious implications for patients scheduled for malignancy resection.

The most common cause of anaemia in the preoperative period (80%) is iron deficiency. In order to distinguish pure iron deficiency anaemia from anaemia of chronic inflammation (with or without iron deficiency) additional tests are required: ferritin concentration, transferrin saturation (TSAT), markers of chronic inflammation (C – reactive protein, CRP). The causes of pure iron-deficiency anaemia include insufficient dietary intake, poor intestinal absorption and blood loss [10]. The sources of blood loss include gastrointestinal (gastrointestinal malignancy), haematuria, menstruation, uterine fibroids. Poor absorption of iron from food may occur in inflammatory bowel disease, celiac disease, deficiency of intrinsic factor (i.e. pernicious anaemia), or following surgery (e.g. gastric bypass). Functional iron deficiency may be present in chronic inflammation. A component of chronic inflammation is present in chronic infection, malignancy, chronic kidney disease, autoimmune disease (e.g. rheumatoid arthritis), and inflammatory bowel disease. The treatment of absolute or functional (chronic disease with iron deficiency) iron deficiency in the preoperative period includes primarily iron supplementation. In our cohort, 15.1% of anaemic patients were diagnosed with microcytic anaemia. Those patients were candidates for iron supplementation, preferably in intravenous form [11].

Although microcytic anaemia may indicate thalassemia, it is an inherited disorder diagnosed in childhood, present mainly in people of Italian, Greek, Middle Eastern, South Asian and African descent. In order to diagnose thalassemia, further testing is required (i.e. HGB electrophoresis, DNA testing). An asymptomatic form of thalassemia that can result in mild anaemia is beta-thalassemia minor. The prevalence of beta-thalassemia minor is estimated to be 1.4% in the Polish population. In order to identify thalassemia, the Mentzer index can be applied [12]. It is a quotient of MCV divided by RBC, with the result less than 13 indicating thalassemia, greater than 13 – IDA. The Mentzer index has high sensitivity and

Tab. I. Selected red blood cell parameters and reference values.

PARAMETER	ABBREVIATION	REFERENCE VALUES
Haemoglobin concentration	HGB	115–150 g/l
Mean Corpuscular Volume	MCV	84–98 fl
Mean Corpuscular Haemoglobin	MCH	27–31 pg
Mean Corpuscular Haemoglobin Concentration	MCHC	32–36 g/dl
Red Blood Cell Distribution Width – Coefficient of Variation	RDW-CV	11.0–16.0 %

Tab. II. Demographic and clinical data of patients.

SEX (M/F)	227/215
Age, median (IQR) [years]	64 (56–70)
Weight, median (IQR) [kg]	72 (62–83)
Height, median (IQR) [m]	1.68 (1.61–1.75)
Body Mass Index, median (IQR) [kg m^2]	25.53 (22.66–28.68)
ASA classification, median (IQR)	3 (2–3)
Type of procedure, n (%):	
- pancreas	256 (58)
- large bowel	46 (10.4)
- stomach	41 (9.3)
- aesophagus	28 (6.3)
- small bowel	24 (5.4)
- biliary tract	24 (5.4)
- liver	18 (4.1)
-other abdominal	5 (1.1)
HGB, median, IQR [g L^{-1}]	134 (122–143)
MCV, median, IQR [fL]	90 (90–93)
MCH, median, IQR [pg]	30,5 (29.1–31.7)
MCHC, median, IQR [g dL^{-1}]	33.7 (33.1–34.3)
RDW-CV, median, IQR [%]	13.7 (13–14.8)

ASA – American Society of Anaesthesiologists, HGB – Haemoglobin, IQR – Interquartile Range, MCH – Mean Corpuscular Haemoglobin, MCHC – Mean Corpuscular Haemoglobin Concentration, MCV – Mean Corpuscular Volume, RDW-CV – Red Blood Cell Distribution Width - Coefficient of Variation

specificity and it can be helpful in deciding on the performance of expensive genetic testing for thalassemia [13].

In our study 4.8% of anaemic patients were diagnosed with macrocytic anaemia. Only 2.4% of all anaemic patients could be accurately diagnosed with vitamin B12/folate deficiency using our simplified diagnostic algorithm.

Altogether 17.5% of anaemic patients in our study were diagnosed with haematinic deficiencies according to the presented diagnostic algorithm. Although a majority of patients with anaemia still required further testing, taking into account numbers of patients undergoing elective procedures it could potentially translate into a large number of patients who could have their anaemia addressed early in preparation for an elective procedure. Time context is very important as more surgeries are scheduled close to pre-anaesthetic clinic visits and there is not enough time for iron/vitamin supplementation. In order to increase haemoglobin concentration in IDA it usually takes 4 weeks. However, re-evaluation after two weeks is required as some patients will not respond to oral supplements.

Avoiding unnecessary diagnostic tests for anaemia in these 17.5% of patients might have saved costs. It is wise to start from CBC and then order further testing for patients in the grey zone.

In our study 73.5% of anaemic patients were normocytic. This category of patients includes patients with chronic disease, chronic inflammation, haemolysis, acute blood loss, bone marrow aplasia and further testing including iron tests (ferritin, transferrin saturation index) and markers of chronic inflammation (C-reactive protein) is warranted. Twenty patients with normocytic anaemia and high RDW values were likely to suffer from some form of haematinic deficiency. Many of these patients would probably benefit from iron supplementation but further testing is required.

CONCLUSIONS

Preoperative anaemia is common in elective gastrointestinal surgery. Simplified diagnostic algorithm based on complete blood count parameters might be helpful in the preliminary identification of patients with iron and vitamin B12/folic acid deficiencies so haematinic supplementation can be started early.

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