The role of immature granulocyte in the early prediction of gastrointestinal tract perforations

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Abstract

Background/Aim: Gastrointestinal system (GIS) perforations cause acute abdomen an indication for emergency intervention. Early detection is very important in gastrointestinal perforations to prevent mortality and morbidity. This study aimed to examine whether immature granulocyte (IG) and IG percentages (IG%) can be used as a simple and easy marker for identifying gastrointestinal system perforations early on.

Methods: Between January 1, 2020, and January 1, 2022, 120 patients who presented to Hitit University Erol Olçök Training and Research Hospital's emergency service and underwent surgery on by the General Surgery Clinic with the diagnosis of the acute abdomen were investigated. The patients were divided into two groups. Patients in group 1 included those with peptic ulcers and bowel perforations. Group 2 was considered the control group. Of the 36 patients in group 2, 22 had acute appendicitis, 12 had ileus-related bridectomy or bowel resection, and two had acute cholecystitis. The common patient feature in this group was full-thickness or serosal iatrogenic bowel injury and repair. Pre-operative IG and IG% values were obtained from routine complete blood count values. IG and IG% values were compared between groups 1 and 2, and the predictive value of these biomarkers in the early diagnosis of GIS perforations was investigated.

Results: The mean age of the patients was 55.49 (19.58). The study consisted of 45 (37.5%) female patients and 75 (62.5%) male patients. Group 1 had 84 patients, whereas Group 2 had 36. When the two groups were evaluated, the IG value was higher in Group 1 ($P < 0.001$). In terms of the percentage value of immature granulocytes, a statistically significant difference was found between Groups 1 and 2 ($P = 0.001$). As a result, Group 1's IG and IG% values were much greater than those in Group 2.

Conclusion: IG and IG% values are inflammatory parameters that can be easily studied in routine hematology tests. According to this study, IG and IG% values were found to be higher in gastrointestinal tract perforations based on result blood tests taken at the time of admission to the emergency department.

Keywords: Gastrointestinal tract, Perforation, Percentage of immature granulocytes, Immature granulocytes

Introduction

Gastrointestinal system (GIS) perforations cause acute abdomen, an indication for emergency intervention. Gastrointestinal tract (GIT) perforation occurs due to peptic ulcer disease, trauma, iatrogenic disease, foreign bodies, appendicitis, inflammation, and/or tumors, which require early diagnosis and timely surgical intervention [1]. Peptic ulcer perforation is the most common cause. The main treatment method for GIT perforation is surgery [2]. To plan the correct treatment, the presence, location, and cause of the perforation should be determined. Diagnosis is made by the presence of free air under the diaphragm on chest X-ray or intra-abdominal fluid or air on computed tomography (CT); in addition, the diagnosis is verified by elevated white blood cell (WBC) and C-reactive protein (CRP) levels. However, in the early stages of perforation, these examinations cannot provide a clear indication. Early diagnosis is significant for preventing mortality and morbidity in perforations. Therefore, a specific biomarker is needed for the early diagnosis of intra-abdominal organ perforation.

Immature granulocytes (IG) in peripheral blood are an indicator of increased bone marrow activation [3]. IG is a newly considered inflammatory marker that can be measured easily in a standard blood count [4, 5]. Studies have shown that IG counts and IG percentages (IG%) are higher than in healthy individuals in cases of sepsis and infection [6]. IG% count showed infection even without leukocytosis [7]. In the current study, the predictive value of IG count and IG percentage for the early diagnosis of GIS perforation was investigated.

Materials and methods

This research was planned as a retrospective cohort study. After receiving approval from Hitit University Faculty of Medicine's Clinical Research Ethics Committee in 2022 (Ethics Committee Decision No:2022-12), 120 patients who presented to the Emergency Service of Hitit University Erol Olçok Training and Research Hospital between January 1, 2020 and January 1, 2022 and underwent surgery in the General Surgery Clinic with the suspicion of the acute abdomen were examined. Inclusion criteria in included several parameters: (1) > 18 years old, (2) admission to the emergency department, and (3) underwent emergency surgery. Patients < age of 18, those who had a disease that may have affected their blood parameters (cirrhosis, chronic kidney failure), those who were scheduled for elective surgery, those who were pregnant or breastfeeding, those who were in a limited population (mental illness patients, soldiers, prisoners), and those whose data could not be accessed were excluded.

The study population was divided into two groups: (1) with GIS perforation during the operation (Group 1) and (2) those who did not (Group 2). Patients in group 1 included peptic ulcer and bowel perforations. Group 2 was planned as the control group. Of the 36 patients in group 2, 22 had acute appendicitis, 12 had ileus-related bridectomy or bowel resection, and two had acute cholecystitis. The common feature of the patients selected in this group was full-thickness or serosal iatrogenic bowel injury and repair

Patients' pre-operative hemogram parameters from the hospital's file system were scanned, and IG count and percentage IG% were recorded. Pre-operative IG and IG% values were compared between groups 1 and 2, and their value for predicting GIS perforations was statistically calculated.

Statistical analysis

Data analysis was performed using the IBM SPSS 22.0 software for Windows. The aim was to examine two separate clinical entities by retrospective analysis. The normality of the data was determined using the Shapiro–Wilk test. Continuous values are given as mean standard deviation (SD) or median and an interquartile range (IQR) of 25% to 75%. Non-parametric values were analyzed using the Mann–Whitney U test and parametric values using the Student's t-test. The optimum threshold values for IG and IG% were calculated by receiver operating curve analysis (ROC). P-values < 0.05 were considered statistically significant.

Results

One-hundred twenty patients who were admitted to the emergency department and underwent surgery were included in the study. Our sample had a mean age of 55.49 (19.58) years. Forty-five (37.5%) patients were female and 75 (62.5%) were male. Group 1 had 84 patients and, Group 2 consisted of 36. The mean age of group 1 subjects was 52 (21.19), and the mean age of group 2 was 63 (12.83). Group 1 consisted of 61 males and 23 females. Fourteen men and 22 women were in group 2. No statistical differences between the two groups in terms of the distribution of age and sex (P = 0.855 and P = 0.714, respectively) were found.

In the comparisons between the groups, the patients showed a non-normal distribution. When comparing the two groups in terms of IG, a statistically significant difference (P < 0.001) was observed. Group 1 had a median IG count of 0.07 (95% IQR 0.0836–0.1911) and Group 2 had a median IG count of 0.04 (95% IQR 0.0319–0.0936). Accordingly, the IG count was significantly higher in Group 1. Similarly, a statistically significant difference between the groups in terms of IG% (P = 0.001) was found. Group 1 had a median IG% of 0.5 (95% IQR 0.6630–1.0917) and Group 2 had a median IG% of 0.35 (95% IQR 0.3428–0.6961). Accordingly, the IG percentage was significantly higher in Group 1 than in Group 2.

In the ROC analysis (Figure 1), the area under the curve (AUC) for IG was 0.711 with 69% sensitivity and 63.9% specificity at a cut-off value of 0.045. The AUC value for IG% was 0.690 with 63% sensitivity and 72.2% specificity using a cut-off value of 0.45 (Table 1).

Our subgroup analysis demonstrated that the most common perforation in Group 1 (n = 84) was peptic ulcer perforation (n = 40) (Table 2). Other perforation areas were small bowel and large bowel perforations. In the evaluation made between them, no statistical difference was observed between IG and IG% values. However, in the examination between any perforation (Group 1) and no perforation (Group 2), IG and IG% values were found to be higher in Group 1 (P < 0.001). From these results, it was thought that the high IG and IG% values were not associated with the localization of the perforation but rather only with the perforation (Tables 3, 4).

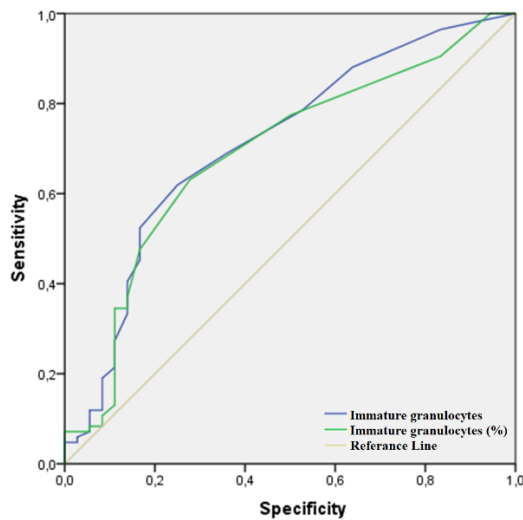Figure 1: ROC Curve for immature granulocytes and immature granulocytes (%)

Table 1: Receiver operating characteristic (ROC) curves obtained for immature granulocytes (IG), and immature granulocytes percentages (IG%)

Variable(s)	AUC	P-value	95% CI Lower Bound	95% CI Upper Bound	Sensitivity	Specificity	Cut-off value
Immature granulocytes	0.711	<0.001	0.608	0.815	69%	63.9%	0.045
Immature granulocytes (%)	0.690	0.001	0.585	0.794	63%	72.2%	0.45

AUC: area under the curve; CI: confidence interval

Table 2: Percentages by perforated areas

	Frequency	Percent
Perforation (-)	36	30.0
Peptic ulcer perforation	40	33.3
Small bowel perforation	25	20.8
Colon perforation	19	15.8
Total	120	100.0

Table 3: Pairwise comparisons; Location of perforation for immature granulocytes

	Std. Error	P-value
Perforation (-) vs Peptic ulcer perforation	7.966	0.092
Perforation (-) vs Small bowel	9.932	0.011
Perforation (-) vs Colon	9.027	0.004
Peptic ulcer perforation vs Small bowel	9.661	1
Peptic ulcer perforation vs Colon	8.840	1
Small bowel vs Colon	10.553	1

Table 4: Pairwise comparisons; Location of perforation for immature granulocytes (%)

	Std. Error	P-value
Perforation (-) vs Peptic ulcer perforation	7.726	0.001
Perforation (-) vs Small Bowel	8.982	0.004
Perforation (-) vs Colon	9.793	0.001
Peptic ulcer perforation vs Small bowel	8.796	0.160
Peptic ulcer perforation vs Colon	9.312	0.984
Small bowel vs Colon	10.5	1

Discussion

IG and IG% are inflammatory parameters that can be easily examined by routine hematology tests. According to the current study, high IG and IG% values were significant for diagnosing GIS perforations early in the course of the disease.

Gastrointestinal (GI) perforation is defined as the disruption of tissue integrity in the GI canal wall due to an ulcer, trauma, foreign body, and/or cancer [8]. GIT perforation is a common medical emergency associated with considerable mortality, which ranges from 30% to 50% [9]. A subset of patients exhibits delayed symptoms, abscess formation that mimics an abdominal mass, and/or sepsis [10]. Diagnosing a GIS perforation can be difficult in cases presenting with nonspecific symptoms. Clinical findings vary based on the perforation site. Esophageal perforations may present with severe chest pain and vomiting, gastroduodenal perforations with acute severe abdominal pain, and colonic perforations with bacterial peritonitis with a slower course and abdominal examination

findings due to localized abscess formation [11]. Physical examination, laboratory findings, and radiological chest and abdominal X-rays are used for the diagnosis of a GIS perforation. The presence of free intraperitoneal gas on a routine radiograph usually indicates bowel perforation. According to previous research, 1 mL of intra-abdominal air under the diaphragm on a chest X-ray suggests GIS perforation [12]. Multi-detector computed tomography (MDCT) is the modality of choice for evaluating a suspected perforation [13]. MDCT is quite useful for assessing extraluminal air [14]. Although the diagnosis of a GIS perforation involves both elevated white blood cell and C-reactive protein levels, these tests are nonspecific, and they are also elevated in other inflammatory conditions. Therefore, no specific hematological parameter for the early diagnosis of GIS perforations is available. In the present study, IG and IG% values were found to be significantly higher in patients with perforation, and it appears to be an effective, easy, and inexpensive biomarker for early diagnosis.

GIS perforations can be observed in either sex. Ilgar et al. [15] examined GIS perforations in both males and females and reported a rate of 57.4% for male patients. It was observed that male patients were more prevalent, constituting 67.5% of our sample. Still, no significant difference between the groups in terms of sex was found as shown in previous studies.

Today, with new analyzer systems, IG and IG% values can be calculated easily [16]. Research has proven that IG can be used as an inflammatory marker [17, 18]. Unal et al. [19] found that IG% was significant for the early diagnosis of acute necrotizing pancreatitis. Dogan et al. [20] demonstrated that acute appendicitis patients with higher IG levels could have a higher possibility of perforation. Senlikci et al. [21] revealed that IG and IG% values were significant for evaluating the presence of ischemic bowel in irreducible inguinal hernias.

In the current study, it was found that IG and IG% values were significantly predictive of GIS perforation. According to our ROC analysis, IG had 69% sensitivity and 63.9% specificity using a cut-off value of 0.045. IG% had 63% sensitivity and 72.2% specificity using a cut-off value of 0.45. As found in previous research, increases in IG and IG% values in inflammatory conditions were found. However, unlike previous studies involving inflammatory diseases, our research is the first in the literature to evaluate GIS perforations.

Ilgir et al. [15] reported that among GIS perforations, gastroduodenal perforations were the most common, and MDCT could detect the perforation site with 82.9% accuracy. In this study, gastric perforations (n = 40) were the most common type of perforation. Assessing the perforation sites as subgroups, it was found that IG and IG% values were again statistically higher in the perforated group. However, they were not effective in determining the perforation site.

Limitations

This study has certain limitations. The first is the small sample size, which could be understandable because this was a single-center study, and only patients diagnosed with a GIS perforation were include. Second, other inflammatory markers were not included. Our study is the first in the literature that evaluates GIS perforation in association with IG, and it could

pave the way for further research with larger and more comprehensive samples and other inflammatory markers.

Conclusion

IG and IG% values are inflammatory parameters that can be easily studied in routine hematology tests. According to this study, IG and IG% values were found to be higher in GIT perforations, such as peptic ulcer and small and large intestinal perforations based on the blood results obtained at the time of admission to the emergency department.

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