Annals of Medical Research

DOI: 10.5455/annalsmedres.2019.11.761 2020;27(1):105-9

Original Article

The predictive value of laboratory factors in evaluating the necessity of surgical treatment in Crohn's disease

Emine Ozlem Gur[1], Elif Saritas Yuksel[2], Selda Haciyanli[1], Cem Cekic[2], Osman Nuri Dilek[1], Mehmet Haciyanli[1]

[1]Katip Celebi University Ataturk Training and Research Hospital, Department of General Surgery, Izmir, Turkey
[2]Katip Celebi University Ataturk Training and Research Hospital, Department of Gastroenterology, Izmir, Turkey

Abstract

Aim: The primary treatment of Crohn's disease (CD) is medical but approximately 70% of all patients with CD undergo surgical intervention throughout their lives. We aimed to determine which parameters can guide decision making before surgical treatment and to determine the effectiveness of the Glasgow prognostic index (GPI) and prognostic nutritional index (PNI) in predicting the necessity of surgery.

Material and Methods: Patients who underwent surgery or medical treatment for CD were matched for age and sex. Group 1: operated patients; Group 2: received medical treatment. Hemogram and biochemistry test results were recorded. Platelet to neutrophil ratio (PNR), Neutrophil to lymphocyte ratio (NLR), and Lymphocyte to monocyte ratio (LMR) were calculated. Patients who had both a serum elevation of CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5 g/dL) were allocated a GPI of 2. Patients with only one of the abnormal values were allocated a GPI of 1, and patients who had neither were allocated a GPI 0. Parameters compared statistically between groups. The value $p<0.05$ was accepted significant.

Results: Of the 104 patients 51 were in Group 1 and 53 were in Group 2. The number of patients with a GPI value of 3 was significantly higher in Group 1 than in Group 2 ($p < 0.05$), as were NLR, protein, albumin, neutrophil, platelet, and CRP levels ($p < 0.05$). The multivariate analysis revealed that albumin and GPI values were independent variables in predicting the likelihood of receiving an operation in CD.

Conclusion: In conclusion, evaluating the necessity of surgical treatment during follow-up for CD, neutrophil, NLR, CRP, albumin, platelet, PNI, and GPI, can be used. If the GPI value is 2 in a patient with CD under follow-up whose albumin levels are low, then surgical treatment should be considered.

Keywords: Crohn's disease; blood test; surgery;medical treatment

INTRODUCTION

Crohn's disease (CD) is a chronic and recurrent bowel disease whose etiology has not been clearly established. CD can involve any part of the gastrointestinal system (GIS) but is most commonly seen in the terminal ileum, jejunum, and colon (1). Although the primary treatment for CD is medical, approximately 70% of all patients with CD undergo surgical intervention throughout their lives. Among them, 70% have to undergo secondary surgical treatment (2). Surgical applications together with immunosuppressive agents form another set of treatment options for CD. Although endoscopy and colonoscopy remain gold standards in the follow-up of CD, such procedures are invasive and can cause complications in practice (3).

In previous studies, various blood parameters have been used to determine the degree of CD and to guide treatment planning during follow-up. Among them, blood values such as neutrophils, leukocytes, lymphocytes, platelets, neutrophil-to-lymphocyte ratio (NLR), and, especially in hemogram, platelet-to-neutrophil ratio (PNR) can be used. It has also been shown that C-reactive protein (CRP) and albumin values can be used to guide follow-up treatment for CD (4-6).

The Glasgow prognostic index (GPI) has been used to predict prognosis, morbidity, and mortality in the pre- and

Received: 22.11.2019 **Accepted:** 17.12.2019 **Available online:** 17.02.2020
Corresponding Author: Emine Ozlem Gur , Katip Celebi University Atatürk Training and Research Hospital, Department of General Surgery, Izmir, Turkey **E-mail:** eozlemgur@yahoo.com

postoperative follow-up of many malignant patients in recent years (7-9). Albumin and CRP values factor into the GPI, and patients are evaluated according to values from 0 to 2.

In recent years, the prognostic nutritional index (PNI) has been used to predict postoperative prognosis, especially before major gastrointestinal surgery (10,11). Lymphocyte and albumin values factor into the PNI, and patients with low PNI values are considered to have a high risk of morbidity after major operations (12).

When complications develop during follow-up for CD, surgical treatment is typically applied. Deciding upon surgical treatment for such patients under elective conditions is difficult for both surgeons and gastroenterologists, given the high incidence of postoperative morbidity and mortality in patients undergoing surgery for CD (13,14). In addition to clinical parameters, laboratory parameters should be used to make decisions about surgical treatment for such patients.

In our study, we sought to identify differences in laboratory parameters among patients in follow-up treatment for CD and undergoing surgical treatment compared to ones not undergoing such treatment. In particular, we aimed to determine which parameter or parameters can guide decision making before surgical treatment and to determine the effectiveness of the GPI and PNI in predicting the outcomes of surgery.

MATERIAL and METHODS

Patients who underwent surgery for CD between 2012 and 2018 and who underwent medical treatment in the gastroenterology clinic of our hospital during the same period were matched for age and sex. The study was approved by the ethics committee of the university. The patients who were operated upon formed Group 1, whereas ones who received medical treatment formed Group 2. The groups were compared according to the determined parameters.

Criteria for inclusion in the study were fourfold: a diagnosis with CD, no other inflammatory disease, being treated for CD (e.g., receiving immunomodulatory or biological treatment), and being preoperative (i.e., for Group 1) or having laboratory tests available while under medical treatment (i.e., for Group 2) or else having laboratory tests available preoperatively (i.e., for Group 1) or during medical treatment (i.e., for Group 2). Exclusion criteria were being under 18 years of age, having had an emergency operation (i.e., for Group 1), and having CD in a region outside the small intestine or colon.

Files containing the patients' demographic and medical information were examined, and their age, sex, years since diagnosis of CD, and region where the CD had settled were recorded. CD-concentrated region was divided into three types: small intestine, large intestine, and combined. Protein (g/dl), albumin (g/dl), CRP, Leukocyte, lymphocyte, platelet, monocyte, neutrophil, and hemoglobin levels recorded. For each patient, PNR was calculated by dividing the platelet count by the neutrophil count, NLR by dividing the neutrophil count by the lymphocyte count, and the lymphocyte-to-monocyte ratio (LMR) by dividing the lymphocyte count by the monocyte count. GPI values were electronically calculated according to CRP and albumin values on the website MDCalc (https://www.mdcalc.com/glasgow-prognostic-score-gps-cancer-outcomes). Patients who had both a serum elevation of CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5 g/dL) were allocated a GPI of 2. Patients with only one of the abnormal values were allocated a GPI of 1, and patients who had neither were allocated a GPI of 0. PNI values were calculated according to the formula PNI = 10x (alb + 0.005x lymphocyte) (12). Both groups were compared statistically in terms of recorded parameters.

Postoperative lengths of hospital stay (LOS) were also recorded for patients in Group 1, and the parameters affecting LOS were evaluated statistically. The duration of hospitalization and factors of the development of complications were also investigated statistically in Group 1 in a subgroup analysis.

Statistical analysis

Student's t test was used for continuous variables, whereas a chi-squared test was used for categorical variables. Values of $p < 0.05$ were considered to be statistically significant. Significant parameters from univariate analysis were evaluated by multivariate analysis. In the evaluation using logistic regression test, values of $p < 0.05$ were considered to be significant as well. One-way analysis of variance test was used for subgroup analysis in Group 1 to evaluate risk factors for complication. The Statistical Package for the Social Sciences version 21.0 was used for statistical analysis.

RESULTS

Of the 104 patients who met the criteria and were included in the study, 51 were in Group 1 and 53 were in Group 2. In Group 1, the mean age was 41.45 ± 11.30 years, and 64.7% (n = 33) were male. In Group 2, 31 patients were male (58.4%), and the mean age was 39.68 ± 14.44 years. No significant difference emerged between the groups in terms of age or sex.

No significant difference surfaced between the groups in terms of CD localization, leukocyte, lymphocyte, monocyte, hemoglobin, PNR, LMR, or time of CD diagnosis, either. The number of patients with a GPI value of 3 was significantly higher in Group 1 than in Group 2 ($p < 0.05$), as were NLR, protein, albumin, neutrophil, platelet, and CRP levels ($p < 0.05$), as shown in Table 1.

The reasons for undergoing surgery among patients in Group 1 were intraabdominal abscess (n = 20), enterocutan or enteroenteric fistula (n = 32), and intestinal stricture (n = 32). Of them, 19 patients (37.2%) experienced postoperative complications; 15 had minor complications (e.g., wound infection), whereas the other four had major ones (e.g., anastomotic leak). One patient underwent reoperation. All the patients in Group 1 were discharged, and the group had no cases of mortality. The

Table 1. The characteristics of the groups

	Group 1 (n: 51)	Group 2 (n:53)	p
Age	41.45±11.307	39.68±14.447	0.13
Gender			0.55
Male	33 (64.7%)	31 (58.4%)	
Female	18 (35.3%)	22 (41.6%)	
Location			0.07
Ilea	15 (29.4%)	26 (49.0%)	
Ileocolic	16 (31.3%)	10 (18.8%)	
colonic	20 (39.3%)	17 (32.2%)	
Protein	6.2±1.1	7.247±0.35	**0.0001**
Albumin	3.30±0.79	4.28±0.31	**0.0001**
CRP*	4.60±5.12	0.85±1.46	**0.0001**
WBC†	8.86±2.98	8.09±2.49	0.18
Neutrophil	6.42±2.92	5.15±1.82	**0.01**
Lymphocyte	1.76±0.75	2.20±1.55	0.10
Platelet	373.5±134.1	286.4±92.6	**0.009**
Monocyte	0.56±0.25	0.57±0.51	0.58
Hgb‡	11.79±1.8	13.6±1.51	0.16
GPI§			**0.001**
0	18 (35.2%)	53 (100%)	
1	12 (23.5%)	0	
2	21 (41.3%)	0	
NLR	5.05±6.66	2.84±1.42	**0.007**
LMR¶	3.83±2.50	4.50±3.24	0.70
PNR**	66.74±33.07	63.66±44.67	0.58
PNI††	32.4803±9.10772	42.9591±3.13737	**0.0001**
Disease Duration	9.17±4.17	8.28±3.51	0.16

*CRP : C reactive protein. †WBC: White Blood Cell, Hgb: hemoglobin ‡, §GPI: Glasgow prognostic index NLR: neutrophil lymphocyte ratio, ¶LMR: lymphocyte monocyte ratio, **PNR: platelet neutrophil ratio, ††PNI: prognostic nutrition index

Table 2. The multivariate analysis of significant parameters

Parameter	Group 1 (n: 51)	Group 2 (n:53)	Significance	OR	CI
Protein	6.2±1.1	7.247±0.35	0.91	0.109	0.145 -0.130
Albumin	3.30±0.79	4.28±0.31	0.05	1.911	0.008-0.428
CRP*	4.60±5.12	0.85±1.46	0.54	0.604	0.031-0.017
Neutrophil	6.42±2.92	5.15±1.82	0.90	0.122	0.000-0.001
Platelet	373.5±134.1	286.4±92.6	0.84	0.194	0.018-0.022
GPI†					
0	18 (35.2%)	53 (100%)	**0.002**	**3.159**	0.394-0.090
1	12 (23.5%)	0			
2	21 (41.3%)	0			
NLR‡	5.05±6.66	2.84±1.42	0.90	0.121	0.044-0.039
PNI§	32.4803±9.10772	42.9591±3.13737	0.337	0.96	

*CRP: C reactive protein, †GPI: Glasgow prognostic index, ‡NLR: neutrophil lymphocyte ratio, §PNI: prognostic nutrition index

parameter affecting the complications was the leucocyte value, whereas the other parameters had no effect on complications.

The overall LOS was 8.1 (3–30) days. Lymphocyte number and NLR values were significantly predictive markers for LOS in Group 1 ($p < 0.05$), whereas the other parameters did not predict LOS in either group.

The multivariate logistic regression test revealed that albumin and GPI values were independent variables in predicting the likelihood of receiving an operation among patients with CD. The risk factor for operation was 3.15 in patients with a GPI value of 2, whereas the risk factor for low albumin value was 1.9 (Table 2).

DISCUSSION

Scoring systems are available to make decisions about surgical treatment for CD and to determine the severity of the disease. In addition to those systems, follow-up entailing endoscopy and colonoscopy remains the gold standard (5,16). In our study, parameters that could inform clinicians about the timing of surgical treatment were evaluated. The parameters used are generally used as acute inflammatory markers in many branches of medicine. Previously, it has been shown that NLR, platelet count, PLR, and PNI values are especially applicable in guiding the follow-up treatment of inflammatory bowel diseases such as CD and ulcerative colitis (4,6,17).

White blood cell count, CRP, and erythrocyte sedimentation ratio (ESR) are the most commonly used inflammatory parameters measured for CD in routine clinical practice. Those parameters may vary according to the degree of inflammation. NLR and PLR, both of which are positively correlated with ESR and CRP (18), are inexpensive and simple proportional parameters to apply, as well as are systemic inflammatory markers that correlate with disease severity and prognosis in CD. NLR is a frequently studied parameter in inflammatory and neoplastic diseases, including colorectal cancer, hepatocellular cancer, multiple myeloma, and inflammatory diseases such as myocardial infarction and ulcerative colitis (19-21). Likewise, NLR can be used as an inflammatory and disease grade marker in cases of CD.

Feng et al. (22) showed that platelet count, NLR, and PLR values used as an inflammatory and disease grade in the general population. Moreover, they found no significant difference in the other inflammatory parameters between the healthy population and patients with CD. In another study, Acartürk et al.(6) observed that NLR, lymphocyte count, neutrophil count, ESR, and white blood cell count, as well as the CRP value, were all significantly higher during the active period of CD. Those authors determined NLR with a 3.2 cutoff value. In our study, neutrophil count, NLR, albumin count, CRP value, and platelet value, all of which may indicate acute inflammatory response, were significantly higher in Group 1. The mean NLR value was 5.05 in Group 1 and 2.84 in Group 2. In another study, Gao et al.(4) detected a significant difference between NLR, CRP value, ESR, and white blood cell count between controls and patients with CD. In addition, as revealed by a comparison of the same parameters between active and inactive CD groups, the CRP value was significantly higher in active group and other parameters did not differ. Fistula, stricture, or abscess appeared in all patients in Group 1 as the pathology causing acute inflammation. In Group 2, inflammatory parameters remained at normal levels, and no pathology requiring any surgical intervention was clinically detected.

GPI is a parameter used to evaluate many malignant patients and often applied in the postoperative period for monitoring purposes, because it indicates the presence of inflammation. Because the GNI is easy to calculate and evaluate, it can be used easily in daily practice. Zhu et al. (23) observed that the rates of postoperative septic complications were higher among patients with high GPI values undergoing bowel resection for CD than among patients with low GPI values. No study on the effectiveness of using GPI among patients with CD in follow-up during the preoperative inactive period was found in our review of English-language literature. In our study, the GPI value among patients with CD requiring surgery was significantly different from that among patients receiving medical treatment. The number of patients with a GPI value of 2 was 0 in Group 2, which suggests that the GPI value can be used for measuring the severity of CD in patients in follow-up.

The PNI value is also used to evaluate the inflammatory process in many diseases. Zhou et al.(24) have shown that postoperative infectious processes were more common in patients with CD who had PNI values of at least 40. In our study, PNI values were significantly higher among patients in Group 1 with inflammation than among Group 2.

When the same parameters were evaluated in multivariate analysis, the GPI value differed by showing the presence of inflammation in patients requiring operation independent of other parameters. By contrast, albumin value was a significant borderline parameter in multivariate analysis. Other parameters found to be significant in univariate analysis were insignificant in multivariate analysis.

A major limitation of our study was the small sample size. A series of studies with more patients could provide more detailed results. Moreover, because the variables evaluated are used to evaluate many inflammatory processes, creating a CD-specific parameter proved impossible. Therefore, other clinical and laboratory findings are needed from evaluations of patients with CD in whom those parameters are significant. However, changes in blood values in patients with CD under follow-up might guide clinicians in making treatment decisions as well.

CONCLUSION

In conclusion, CD is an essentially medically treated inflammatory bowel disease. While evaluating the necessity of surgical treatment during follow-up for CD, endoscopy, colonoscopy, and the assessment of physical parameters and inflammatory parameters, including neutrophil count, NLR, CRP value, albumin count, platelet

count, PNI, and GPI, can be used. If the GPI value is 2 in a patient with CD under follow-up whose albumin levels are low, then surgical treatment should be considered. Indeed, a GPI value of 2 for patients with low albumin values can be used by itself as an indicator of inflammation in patients with CD.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports.
Ethical approval: There is approvel of ethic commity of our hospital.

Emine Ozlem Gur ORCID: 0000-0003-2749-2220
Elif Saritas Yuksel ORCID: 0000-0003-1104-3041
Selda Haciyanli ORCID: 0000-0002-5956-8421
Cem Cekic ORCID: 0000-0002-1964-8240
Osman Nuri Dilek ORCID: 0000-0002-6313-3818
Mehmet Haciyanli ORCID: 0000-0002-0512-1405

REFERENCES

1. D. C. Baumgart and W. J. Sandborn, "Crohn's disease," Lancet 2012;380:1590-605.
2. Landsend E, Johnson E, Johannessen HO, Carlsen E. Long term outcome after intestinal resection for Crohn's disease. Scand J Gastroenterol 2006; 41:1204-8.
3. James WT Toh, Peter Stewart, Matthew JFX Rickard, et al. Indications and surgical options for small bowel, large bowel and perianal Crohn's disease. World J Gastroenterol 2016;22:8892-904.
4. Sheng-Qiang Gao, Li-Dong Huang, Rui-Jie Dai, et al. Neutrophil-lymphocyte ratio: a controversial marker in predicting Crohn's disease severity. Int J Clin Exp Pathol 2015;8:14779-85.
5. Hiroshi Takeyama, Tsunekazu Mizushima, Hideki Iijima, et al. Platelet Activation Markers Are Associated with Crohn's Disease Activity in Patients with Low C-Reactive Protein. Dig Dis Sci 2015;60:3418-23.
6. Acarturk G, Acay A, Demir K, et al. Neutrophil-to-lymphocyte ratio in inflammatory bowel disease. As a new predictor of disease severity. Bratisl Lek Listy 2015;116; 213-7.
7. Shibutani M, Maeda K, Nagahara H, et al. Prognostic Significance of the Preoperative Ratio of C-Reactive Protein to Albumin in Patients with Colorectal Cancer. Anticancer Res. 2016;36:995-1001.
8. Yamada S, Fujii T, Yabusaki N, et al. Clinical Implication of Inflammation-Based Prognostic Score in Pancreatic Cancer: Glasgow Prognostic Score Is the Most Reliable Parameter. Medicine (Baltimore) 2016;95:3582.
9. Chen H, Hu N, Chang P, et al. Modified Glasgow prognostic score might be a prognostic factor for hepatocellular carcinoma: a meta-analysis. Pan Minerva Med 2016.
10. Dai Y, Fu X, Li T, et al. Long-term impact of prognostic nutritional index in cervical esophageal squamous cell carcinoma patients undergoing definitive radiotherapy. Ann Transl Med 2019;7:175.
11. Luvián-Morales J, González-Trejo S, Carrillo JF, et al. Association of the prognostic nutritional index and overall survival in patients with colorectal cancer: A STROBE compliant retrospective cohort study. Cancer Med 2019.
12. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi. 1984;85: 1001-5.
13. Bednarz W, Czopnik P, Wojtczak B, Olewiński R, Domosławski P, Spodzieja J. Analysis of results of surgical treatment in Crohn's disease. Hepatogastroenterology 2008;55:998-1001.
14. Frolkis AD, Dykeman J, Negrón ME, et al. Risk of surgery for inflammatory bowel diseases has decreased over time: a systematic review and metaanalysis of population-based studies. Gastroenterology 2013; 145:996-1006.
15. Bruining DH and Loftus EV. Current and future diagnostic approaches: from serologies to imaging. Curr Gastroenterol Rep 2007;9:489-96.
16. Naber AH and de Jong DJ. Assessment of disease activity in inflammatory bowel disease; relevance for clinical trials. Neth J Med 2003;61:105-10.
17. Rachmilewitz D. Coated mesalazine (5-aminosalicylic acid) versus sulphasalazine in the treatment of active ulcerative colitis: a randomised trial. BMJ 1989;298: 82-6.
18. Khan K, Schwarzenberg SJ, Sharp H, et al. Role of serology and routine laboratory tests in childhood inflammatory bowel disease. Inflamm Bowel Dis 2002;8:325-9.
19. Núñez J, Núñez E, Bodí V, et al. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in ST segment elevation myocardial infarction. Am J Cardiol 2008;101:747-52.
20. Walsh SR, Cook EJ, Goulder F, et al. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. J Surg Oncol 2005;91:181-4.
21. Friedman GD, Tekawa I, Grimm RH, et al. The leucocyte count –correlates and relationship to coronary risk factors – the CARDIA study. Int J Epidemiol 1990;19: 889-93.
22. Feng JR, Qiu X, Wang F, et al. Diagnostic Value of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Crohn's Disease. Gastroenterol Res Pract 2017;2017:3526460.
23. Zhu Y, Xu H, Liu W, et al. Glasgow prognostic score is a practical predictive index for postoperative intra-abdominal septic complications after bowel resection in Crohn's disease patients. Int J Colorectal Dis 2018 ;33:947-53.
24. Zhou W, Cao Q, Qi W, et al. Prognostic Nutritional Index Predicts Short-Term Postoperative Outcomes After Bowel Resection for Crohn's Disease. Nutr Clin Pract 2017;32:92-7.