

Comorbidities and Other Predictors for Severity of Colonic Diverticulitis?

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Received: 17 Mar 2021

Accepted: 07 Apr 2021

Published: 13 Apr 2021

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Keywords:

Diverticulitis; Severity; Hinchey Classification; Ambrosetti's Classification; Charlson's Comorbidity Index

Citation:

Yeşiltaş M, Comorbidities and Other Predictors for Severity of Colonic Diverticulitis?. Clin Surg. 2021; 5(6): 1-9

1. Abstract

1.1. Background: Predicting severity of acute colonic diverticulitis (ACD) is important for management, morbidity and mortality. The aim of this study is evaluating the Charlson's Comorbidity Index (CCI) as severity predictor of ACD.

1.2. Methods: This is a retrospective cohort study. The hospitalized patients for ACD between 01 January 2015 and 01 January 2020 evaluated for study. The patients age, gender, Length of Stay (LOS), colonic location, treatment, levels of C-Reactive Protein (CRP), White Blood Cell (WBC), Neutrophil, Neutrophil Percentage (Neu, Neu%), neutrophil to lymphocyte ratio (NLR), CCI, and survive results evaluated according to Hinchey (HC) and Ambrosetti's Classification (AC) retrospectively.

1.3. Results: 127ACDpatients were included to study. 44,8% were male, and the mean age was 57.6(13.4) years. 87.4% of the ACD was left sided. The most common HC was HC1 with 70.8%, and 4.8% of the ACD was HC4. 24.7% of the ACD was severe. The most common treatment was medical (74%), subsequent hart man procedure (14.2%). 5.5% of the ACD had recurrent disease, and 3.2%of the ACD died. >50 years, LOS, treatment, complication, survive, CRP, Neu%, Neu, NLR was significantly different between HC groups (p:0.001, p<0.0001, p<0.0001, p<0.0001, p:0.001, p:0.001, p:0.006, p<0,0001 respectively). LOS, treatment, complication, survive, CRP, Neu%, Neu, NLR found significantly different between AC groups (p<0.0001, p<0.0001, p<0.0001, p<0.0001, p<0.0001, p<0.0001, p:0.005, p: 0,001 respectively).

CCI was not significantly different at both HC and AC (p:0.147, p:0.087 respectively).

1.4. Conclusions: Comorbidities can be facilitator of severe or complicated ACD, but >50 years old, male gender, left sided, higher CRP, Neu% Neu, and NLR could be good predictors of severe or complicated ACD.

2. Introduction

Diverticulum of colon (DC) is a herniation of mucosa and submucosa due to increased colonic pressure [1]. The incidence of DC reported as 20% under 50 years, and increased to 75% over 80 years [2]. Older age, lower fiber intake, obesity and smoking are the risk factors for DC [3]. Most of the DC is asymptomatic, only diverticulitis (ACD) developed at 4% of the DC all their lifetime [4]. 1-2% of the symptomatic DC requires hospitalization and 0.5% surgery. DC more than 90% occurs at sigmoid and descending colon. The left sided DC seen generally at western countries, however the right sided DC at Asian countries [5].

The severity of ACD managed as uncomplicated or complicated, mild or severe by Ambrosetti, orseverity classified I to IV by Hinchey [6-8]. First or second episode of ACD reported as a risk for severe ACD than more episodes. Severity risk of age is still contradiction, <50 years or >70 years reported as a risk for severe ACD in literature. Comorbidities reported as a predictive of severe ACD, such as Charlson's Comorbidity Index (CCI) ≥ 3 . Immune suppression, non-steroid anti-inflammatory drugs or steroid intake reported as a predictor of severe ACD. C-Reactive protein (CRP)

>150 mg/L is another predictor of severity in the literature [9].

Predicting severity of ACD is important for appropriate treatment. The uncomplicated ACD could be treated with oral antibiotics as well as outpatient. However surgical intervention needed for the complicated ACD [10, 11]. Severity of ACD also effect the complication, morbidity and mortality rate [12]. The aim of this study is comparing the severity predictors of acute diverticulitis according to two well-known severity classification.

3. Methods

After receiving institutional approval from the ethics committee of Okmeydanı Training and Research Hospital (23 May 2017 date and 669 number), accesable patients records between 01 January 2015 and 01 January 2020, who hospitalized and treated for acute colonic diverticulitis, evaluated retrospectively. Meckel or small intestinal diverticulitis excluded from the study.

Age, gender, Length of Hospital Stay (LOS), Computed Tomography (CT), colonoscopy, location of diverticulum, Hinchey Classification (HC), Ambrosetti’s Clasification (AC), treatment, recurrence, levels of C-Reactive Protein (CRP), White Blood Cell (WBC), neutrophil, neutrophil percentage (Neu, Neu%), Neutrophil to Lymphocyte Ratio (NLR), differential diagnosing, comorbidity, complication, Charlson’s Comorbidity Index (CCI), and

survive results evaluated according to HC and AC retrospectively. Age (years), LOS (days), CRP (mg/dl), Wbc (106/uL), Neu (103/uL) and Neu% measured as Mean (SD). Age also evaluated as <50 years or >50 years, gender evaluated as male or female. CT evaluated as diverticulitis reported on CT yes or no. Performed colonoscopy evaluated as yes or no. Location of diverticulum evaluated as none, left colon, right colon, and both left and right colon. Treatment evaluated as Medical, percutaneous drainage (PD), diagnostic laparoscopy and drainage (DL+ D), hartmann procedure, resection anastomosis (RA), resection anastomosis and diversion (RA+ D). NLR calculated by dividing neutrophil count with lymphocyte count.

Description of Hinchey (HC) and Ambrosetti’s classification (AC) is given at Table 1 [7, 8]. AC evaluated as mild or severe, HC evaluated as I to IV. Charlson’s Comorbidity Index scores is given at Table 2 [13]. The results additionally evaluated due to HC and AC. The statical analysis performed with SPSS 15.0. (IBM Corp., Armonk, NY, USA), age, LOS, laboratory results reported as Mean (SD). Nonparametric values evaluated with Kruskal Wallis, Mann Whitney U, and parametric values evaluated with T-Test, ANOVA, and p<0.05 was accepted as significant.

Table 1: Description of Hinchey and Ambrosetti’s Classification [7, 8]

Stage	Description
Hinchey Classification	
I	Diverticulitis with pericolic abscess
II	Diverticulitis with pelvic abscess and localised abscess
III	Diverticulitis with purulent peritonitis
IV	Diverticulitis with fecaloid peritonitis
Ambrossetti’s Classification	
Mild	Wall thickening >5 mm Pericolic fat standing
Severe	Abscess Extraluminal air Extraluminal contrast

4. Results

From the 151 hospitalized diverticulitis patients, 127 ACD patients included to study. The mean age was 57.6 (13.4) years, 38.6% (n:49) of the ACD patients age was <50 years. 55.2% of the patients was female. The mean LOS was 5.6 (9.3) days. 98.4% (n:125) of the patients had diverticulitis on CT, and 48% (n:61) of the patients performed colonoscopy. 87.4% of the ACD located at left colon, 7.9% at right colon, and 3.9% at both left and right colon. 70.8% of the ACD was HC1, 10.2% was HC2, 14.2% was HC3, and 4.8% was HC4. 74% of the ACD treated medically, 14.2%

with hartmann procedure, and 6.3% with DL+D. 5.5% of the ACD had recurrence disease. The mean of CRP was 152,78 (122,5) mg/dl, Wbc as 13,4 (4,3) 106/uL, Neu% as 75.5 (11,8) %, Neu as 10.3 (4.2) 103/uL, NLR as 7.9 (6.5). The most common differential diagnosing was tumor with 5 patients’, subsequently inflammatory bowel disease with 3 patients’. The most common comorbidities were hypertension (28.3%), and diabetes (14.2%). The most common complication was wound infectious (7.1%). The most common CCI score was 0 (30.6%), and 1 (20.5%). 3.2% (n:4) of the patients was died (Table 3).

Table 2: Charlson’s Comorbidity Index [13]

1 point	Myocardial infarction
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2 points	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumor
	Leukemia
	Lymphoma
3 points	Moderate or severe liver disease
6 points	Metastatic solid tumor
	AIDS*
1 point	50-59
2 points	60-69
3 points	70-79
4 points	>80

Table 3: The Demographic Distribution of Diverticulitis

Parameters			
Age (years)*	57,6 ± 13,4		
	n	%	
≤50 years	49	38,6	
>50 years	78	61,4	
Gender	n	%	
	Male	57	44,8
	Female	70	55,2
LOS (days)*	5,6 ± 9,3		
Diverticulitis on CT	n	%	
	Yes	125	98,4
	No	2	1,6
Performed Colonoscopy	n	%	
	Yes	61	48
	No	66	52
Location of Diverticulum	n	%	
	Left Colon	111	87,4
	Right Colon	10	7,9
	Left and Right Colon	5	3,9
	None	1	0,8
Hinchey Classification	n	%	
	1	90	70,8
	2	13	10,2
	3	18	14,2
	4	6	4,8
Ambrosetti’s Classification	n	%	

Mild	97	76,3
Severe	30	24,7
Treatment	n	%
Medical	94	74
PD	3	2,4
DL+D	8	6,3
Hartmann	18	14,2
RA	1	0,8
RA + D	3	2,4
CRP*	152,78 ± 122,5	
Wbc*	13,4 ± 4,3	
Neu%*	75,5 ± 11,8	
Neu*	10,3 ± 4,2	
NLR*	7,9 ± 6,5	
Differential Diagnosis	n	%
Tumor	5	3,9
IBD	3	2,4
Panniculitis	1	0,8
Appandigitis	1	0,8
Comorbidities	n	%
HT	36	28,3
DM	18	14,2
COPD	8	6,3
CAD	7	5,5
Hypothroidi	7	5,5
CVA	6	4,7
CRF	3	2,4
Hyperchortizolemia	3	2,4
Malignancy	2	1,6
Complications	n	%
Wound Infection	9	7,1
Wound Dehiscence	3	2,4
MOF	2	1,6
Others	4	3,2
CCI Score	n	%
0	39	30,7
1	26	20,5
2	19	15
3	14	11
4	14	11
5	12	9,4
6	2	1,6
10	1	0,8
Recurrence	n	%
	7	5,5
Survive	n	%
Alive	123	96,8
Exitus	4	3,2

*Mean ± Standard Derivation. LOS: Length of hospital stay, CT: Computed Tomography. PD: Percutaneous drainage, DL+D: Diagnostic laparoscopy + drainage, PS+D: Primer suture + drainage, RA: Resection and anastomosis, RA+D: Resection and anastomosis+ diversion. CRP: C-Reactive protein (mg/dl), Wbc: White blood cells (106/uL), Neu%; Neutrophil% Neu; Neutrophil (103/uL) and NLR; Neutrophil to Lymphocyte ratio.

IBD: Inflammatory Bowel Disease, HT: Hypertension, DM: Diabetes Mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary arterial disease, CVA: Cerebrovascular accident, CRF: chronic renal failure, MOF: Multiorgan failure, DVT: Deep venous thrombosis.

Evaluation the results according to HC, the mean age was 54.9 (15) years for the HC1, 64.9 (12.3) years for HC2, 59.3 (13.7) years for HC3, and 56.6 (14.7) years for HC4. The difference of age was not statistically significant between HC groups(p:0.111). However, the difference at ≤50 or >50 years was statistically significant (p:0.012). Female was the most common gender for all HC except HC4 but the difference was not statistically significant between HC groups (p:0.291). The mean LOS was 3.5 (1.5) days for the HC1, 7 (4.1) days for the HC2, 13.2 (22.7) days for the HC3, and 10.6 (7, 6) days for the HC4. The difference of LOS was statistically significant between HC groups (p:0.001). Diverticulitis on CT didn't report only 2 patients' at HC1(p:0.459). The most common performed colonoscopy group was HC1 with 54.4% ratio, but the difference at colonoscopy due to HC was not statistically significant (p:0.852). Right colon located ACD seen only at HC1, left colon located seen only at HC3 and HC4, however the difference was not statistically significant between HC groups (p:0.679). All HC1 patient's, 4 patients' from HC2 treated medi-

cally. Other HC2 patient's performed drainage (percutaneous or surgical). All HC4 patient's performed hartmann procedure. The difference for treatment was statistically significant between HC groups (p<0.0001). Complication didn't report only at HC1, and the difference for complication was statistically significant between HC groups (p<0.0001). The most common CCI score was 1 and seen at HC1. The highest scores were 6 and 10, which seen at HC1. Half of (3/6) HC4 patients had score 2. The difference for CCI was not statistically significant between HC groups (p:0.147). 2 patients' from HC3, and 2 patients' from HC4 died. The difference for survive was statistically significant between HC groups (p:0,0001). The highest CRP, Wbc, Neu levels seen at HC3, subsequent HC2. Neu% increased by increased HC, the difference for CRP, Neu%, Neu, NLR was statistically significant between HC groups (p:0.001, p:0.001, p:0.006, p:0.0001 respectively), however the difference for Wbc was not statistically significant between HC groups (p:0.059) (Table 4).

Table 4: Results of Diverticulitis According to Hinchey Classification

Parameters		Hinchey Classifications					p
		HC1	HC2	HC3	HC4	Total	
Age (years)*		54,9 ± 15,0	64,9 ± 12,3	59,3 ± 13,7	56,6 ± 14,7	57,6 ± 13,4	0,111
≤50 years		41	3	4	1	49	0,012
>50 years		49	10	14	5	78	
Gender	Female	48	10	10	2	70	0,771
	Male	42	3	8	4	57	
LOS (days)*		3,5 ± 1,5	7 ± 4,1	13,2 ± 22,7	10,6 ± 7,6	5,6 ± 9,3	0,001
Diverticulitis on CT	Yes	88	13	18	6	125	0,459
	No	2	0	0	0	2	
Colonoscopy	Yes	41	7	10	3	61	0,852
	No	49	6	8	3	66	
Location of Diverticulum	None	1	0	0	0	1	0,679
	Left Colon	75	12	18	6	111	
	Right Colon	10	0	0	0	10	
	Left and Right Colon	4	1	0	0	4	
Treatment	Medical	90	4	0	0	94	<0,0001
	PD	0	3	0	0	3	
	DL+D	0	6	2	0	8	
	Hartmann	0	0	12	6	18	
	RA	0	0	1	0	1	
	RA + D	0	0	3	0	3	
Complication	Yes	0	3	6	4	13	<0,0001
	No	90	10	12	2	114	

CCI	0	35	1	2	1	39	0,147
	1	18	2	6	0	26	
	2	10	2	4	3	19	
	3	9	3	1	1	14	
	4	10	1	2	1	14	
	5	6	3	3	0	12	
	6	1	1	0	0	2	
	10	1	0	0	0	1	
Survive	Alive	90	13	16	4	123	<0,0001
	Exitus	0	0	2	2	4	
CRP*		117,23 ± 93,4	208,42 ± 117,7	291,64 ± 122,0	148,96 ± 196,5	152,78 ± 122,5	0,001
Wbc*		12,9 ± 3,9	14,9 ± 5,3	15,5 ± 4,6	12,0 ± 4,4	13,4 ± 4,3	0,059
Neu%*		72,9 ± 12	77,5 ± 9,5	83,1 ± 6,7	87,8 ± 6,9	75,5 ± 11,8	0,001
Neu*		9,5 ± 3,8	11,8 ± 5	13 ± 4,3	10,8 ± 4,3	10,3 ± 4,2	0,006
NLR*		5,8 ± 4,8	9 ± 7,8	10,9 ± 7,8	16,5 ± 9,8	7,9 ± 6,5	<0,0001

* Mean ± Standard Derivation. LOS: Length of hospital stay, PD: Percutaneous drainage, DL+D: Diagnostic laparoscopy + drainage, PS+D: Primer suture + drainage, RA: Resection and anastomosis, RA+D: Resection and anastomosis+ diversion. CCI: Charlson’s Comorbidity Index. CRP: C-Reactive protein (mg/dl), Wbc: White blood cells (106/uL), Neu%; Neutrophil%, .Neu; Neutrophil (103/uL) and NLR; Neutrophil to Lymphocyte ratio

Evaluation the results according to AC, the mean age was 55.9 (14.8) years at mild ACD, 58.9 (14.5) years at severe ACD, but the difference at mean age and ≤50 or >50 years was not statistically significant (p:0.341, p:0.51, respectively). 56.7% (n:55) of the mild, 50% (n:15) of the severe ACD was female, but the difference was not statistically significant (p:0.521). The mean LOS was 3.7(1.8) days at mild, 11.7 (17.9) days at severe, and the difference was statistically significant (p<0.0001). Diverticulitis on CT didn’t report at 2% (n:2) of the mild ACD (p:0.682). 47.4% (n:46) of the mild, 50% (n:15) of the severe ACD performed colonoscopy (p:0.961). The most common side of the ACD was left colon for both groups, 90% (n:10) of the right colon side occurred at mild ACD (p:0.506). The medical treatment was performed only mild

ACD, and 3.1% (n:3) of the mild ACD treated with PD. Hartmann was the most common treatment at severe ACD with 60% rate. The difference for treatment between groups was statistically significant (p<0.0001). Complications seen only severe ACD and the difference was statistically significant (p<0.0001). The most common CCI score for mild was 0 with 35% (n:34) rate, for severe was 2 with 23.2% (n:7) rate (p:0.087). All of the death patients were from severe ACD, and the difference was statistically significant (p<0.0001). The mean of CRP, Neu%, Neu, and NLR were higher at severe ACD, and the differences were statistically significant (p<0.0001, p<0.0001, p:0.005, and p:0.001 respectively). The mean of Wbc was higher at severe ACD, but the difference was not statistically significant (p:0.153) (Table 5).

Table 5: Results of Diverticulitis According to Ambrosetti’s Classification

		Mild	Severe	Total	p
Age		55,9 ± 14,8	58,9 ± 14,5	57,6 ± 13,4	0,341
	≤50 years	42	7	49	0,51
	>50 years	55	23	78	
Gender	Female	55	15	70	0,521
	Male	42	15	57	
LOS		3,7 ± 1,8	11,7 ± 17,9	5,6 ± 9,3	<0,0001
Diverticulitis on CT	Yes	95	30	125	0,682
	No	2	0	2	
Performed Colonoscopy	Yes	46	15	61	0,961
	No	51	15	66	

Location of Diverticulum	None	1	0	1	0,506
	Left Colon	83	28	111	
	Right Colon	9	1	10	
	Both Left and Right Colon	4	1	5	
Treatment	Medical	94	0	97	<0,0001
	PD	3	0	3	
	DL+D	0	8	8	
	Hartmann	0	18	18	
	RA	0	1	1	
	RA+ D	0	3	3	
Complication	Yes	0	13	13	<0,0001
	No	97	17	114	
CCI Score	0	34	5	39	0,087
	1	20	6	26	
	2	12	7	19	
	3	10	4	14	
	4	11	3	14	
	5	7	5	12	
	6	2	0	2	
	10	1	0	1	
Survive	Alive	97	26	123	<0,0001
	Exitus	0	4	4	
CRP*		120,6 ± 92,9	256,7 ± 148,2	152,8 ± 122,5	<0,0001
Wbc*		13,1 ± 4,2	14,4 ± 4,4	13,4 ± 4,3	0,153
Neu%*		73 ± 13,9	83 ± 6,5	75,5 ± 11,8	<0,0001
Neu*		9,7 ± 4	12,2 ± 4,1	10,3 ± 4,2	0,005
NLR*		6,1 ± 5,5	11,5 ± 7,9	7,9 ± 6,5	0,001

* Mean ± Standard Derivation. LOS: Length of hospital stay, PD: Percutaneous drainage, DL+D: Diagnostic laparoscopy + drainage, PS+D: Primer suture + drainage, RA: Resection and anastomosis, RA+D: Resection and anastomosis+ diversion. CCI: Charlson’s Comorbidity Index. CRP: C-Reactive protein (mg/dl), Wbc: White blood cells (106/uL), Neu%; Neutrophil%, Neu; Neutrophil (103/uL) and NLR; Neutrophil to Lymphocyte ratio

5. Discussion

Predicting the severity of diverticulitis is important for management, morbidity and mortality. Uncomplicated or mild or Hinchey I diverticulitis managed with anti-biotherapy and sometimes outpatient. Complicated or severe or Hinchey II, III and III diverticulitis required percutaneous or surgical drainage, surgical resection with or without diversion. Older age, left sided, CCI score >3, higher CRP, Wbc, and NLR levels are reported severity predictors of ACD in the literature [14-23].

Development of colonic diverticulum increased with age and reached to 75% at age of 80, however diverticulitis occurred only 10-20% of them. Ambrosetti et al. [7] reported age >70 years, conversely Lorimer et al. [14], and Hall et al. [15] reported age< 50 years as a predictor of severe diverticulitis. In our study 72.9%

(n:78) of the ACD age was >50 years, and 29.5% (n:23) of them was complicated. The difference of age was not significant predictor of severity for AC, but significant for HC. Also treatment and CCI scores were significantly different from under or over 50 years’ age.>50-year age could be severity predictor of CD.

The average risk of female for severe diverticulitis reported as 21%, and male as 25% [16]. Kim et al. [17] reported male gender as a predictor of severity. In our study the average risk of female and male for severe diverticulitis found similar with literature as 21.4% vs. 26.3% for AC. 71.9% of the males, 75.7% of the females were HC1, however 7% of the males, 2.9% of the females were HC4. Male gender could be a non-significant severity predictor of CD.

Left sided diverticulitis seen more than 90% at western countries,

however right sided diverticulitis seen 70% at eastern countries. Left sided diverticulitis seen at elder patients with more complicated than right sided with approximately 40% rate [17,18]. In our study 81,1% of the diverticulitis seen at left side. 93% of the right sided CD was HC1, 86,7% of the right sided CD was mild. 20,9% of the CD was HC3 and HC4, and all of them was left sided. 96,7% of the severe CD was left sided for AC. Left sided could be severity predictor of CD.

Comorbidities were an important facilitator of AD. Chapman et al. reported 70% of CD had comorbidities as cardiovascular disease (HT) (41%), pulmonary disease (23%) and diabetes (11%) [19]. Lorimer et al. reported that CD ratio increased from 47,8% to 76% at the patients with 1-2 or ≥ 3 CCI scores [14]. In our study HT was the most common comorbidities with 28.3% ratio. 30.7% (n:39) of the all patients had 0 CCI score (12.8% (n:5) severe), 35.4% (n:45) had score 1-2 (28.8% (n:13) severe), and 33.9% (n:43) had ≥ 3 scores (27.9% (n:12) severe) at AC. 7.7% (n:3) of the 0 CCI score patient, 28.8% (n:13) of the 1-2 CCI score patient, and 18.6 (n:8) of the ≥ 3 CCI score patient were HC3 and HC4. The difference at CCI was not statistically significant. Comorbidities could be a facilitator of CD but not be a severity predictor of CD.

ACD is an inflammatory disease and many inflammatory biomarkers levels increased such as CRP, Wbc, and Neu%. CRP reported as a severity predictor of CD in previous studies. 150-170 mg/dl cut off level of CRP at CD had 80-90% sensitivity and 65-90% specificity [20, 21]. Increased Wbc, Neu count and Neu% reported at CD in literature. Reynolds et al. reported 13.85x10⁹/l cut off level of Wbc had 44.4% sensitivity, and 71.43% specificity, 11.25 cut off level of Neu count had 42.2 % sensitivity, and 82.14% specificity at CD [22]. Mari et al. reported >6.68 cut off level of NLR had 68.75% sensitivity, and 79.21% specificity at CD [23]. In our study the difference at CRP, Neu, Neu%, and NLR for both AC and HC were statistically significant. Wbc was higher at CD but the difference was not statistically significant. CRP, Wbc, Neu, Neu %, and NLR could be severity predictors of CD.

The limitations of this study were being retrospective, lower numbers of patients especially Hinchey 4, lack of colonoscopy results. Prospective randomized clinical trials should be better for further evaluations.

6. Conclusion

Predicting severity of complicated or severe diverticulitis is important for management, morbidity and mortality. There is controversy with literature >50 years' age and male gender were good predictors of complicated diverticulitis. Along with changing in the literature of eastern and western countries, left sided could be more related with complicated diverticulitis in western countries. Comorbidities can be facilitator, but not a predictor of complicated diverticulitis. Higher CRP, Neu, Neu%, and NLR could be good predictors of complicated diverticulitis.

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