Preoperative Neutrophil-to-Lymphocyte Ratio Is Correlated with Severe Postoperative Complications After Emergency Surgery for Ulcerative Colitis

Kiyoshi Maeda[1], Hisashi Nagahara[1], Masatsune Shibutani[1], Tatsunari Fukuoka[1], Yasuhito Iseki[1], Shinji Matsutani[1], Takahiro Toyokawa[1], Hiroaki Tanaka[1], Kazuya Muguruma[1], Hirokazu Yamagami[2], Kosei Hirakawa[1], Masaichi Ohira[1]

[1]*Department of Surgical Oncology and* [2]*Department of Gastroenterology, Osaka City University Graduate School of Medicine, Osaka, Japan*

Introduction: The incidence of postoperative severe complications is reported to be high in patients undergoing emergency surgery for severe ulcerative colitis (UC). It has also been reported that the preoperative inflammatory status is associated with the frequency of postoperative complications. The neutrophil-to-lymphocyte ratio (NLR) is a simple and useful parameter for determining the inflammatory status.

Methods: In the present study, we retrospectively investigated the correlation between the NLR and the incidence of severe postoperative complications in patients undergoing emergency surgery for severe UC. A total of 105 UC patients who underwent emergency or semi-emergency surgery were enrolled. Various clinical factors and NLR values were evaluated to identify the risk factors for severe complications. Postoperative complications were stratified by their severity according to the Clavien-Dindo Classification (CD). A postoperative complication of CD IIIb or higher was defined as severe postoperative complications. The incidence of severe complications was 16.2%.

Results: A multivariate analysis revealed the ASA score, toxic megacolon, and NLR to be independent risk factors for severe postoperative complications.

Corresponding author: Kiyoshi Maeda, MD, PhD, Department of Surgical Oncology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka, Japan.

Tel.: +81 66645 3838; Fax: +81 66646 6450; E-mail: m1378386@med.osaka-cu.ac.jp

Conclusions: The results of this retrospective study suggest that the NLR is an independent risk factor for severe postoperative complications in patients undergoing emergency surgery for UC.

Key words: Ulcerative colitis – Neutrophil-to-lymphocyte ratio – Postoperative complication

Ulcerative colitis (UC) is a chronic inflammatory disease of the colon. Recent developments in medical therapies, including treatment with anti–tumor necrosis factor (TNF)α antibodies, immuno-modulators, and steroids, have markedly improved the clinical outcomes of patients with UC.[1–7] Although most patients are managed successfully with the above treatments, some patients develop a severe acute attack, which can be life-threatening.[8] Surgical treatment is indicated for UC patients who do not respond to medical therapy or who develop toxic megacolon or perforation of the colon. Total colectomy with ileostomy is usually performed for UC patients with such an acute life-threatening status. The postoperative morbidity and mortality rates associated with emergency surgery in such patients are reported to be 2% to 3% and 30% to 60%, respectively, which are significantly higher than those in the patients who are treated with elective surgery.[9–13] Thus, to avoid delayed surgery, an accurate evaluation of disease severity is important because it allows for the early identification of patients in whom intensive medical treatment is likely to fail and those who will need rescue surgery.

Disease severity is usually assessed based on serum inflammation marker levels. C-reactive protein (CRP), erythrocyte sedimentation, (ESR), white blood cell (WBC) count, and serum level of albumin are commonly used[14,15] but have only moderate accuracy in reflecting the UC disease severity. Thus, the adjunctive use of additional serum markers that will be more sensitive and specific for determining the disease activity and for predicting the patients who require emergency surgery at the proper period is strongly needed in daily clinical practice.

The serum neutrophil-to-lymphocyte ratio (NLR) is a simple marker of subclinical inflammation that can easily be obtained from the differential WBC count.[16] The NLR has been reported to be useful for predicting the outcomes in patients with solid malignancies, inflammatory disease, and coronary artery disease.[17–24] Recently, several studies have reported that the NLR is an indicator of the overall inflammatory status and is a useful predictor of disease severity in UC patients.[25–27] Moreover, it has been shown that the NLR is superior to WBC in predicting adverse outcomes in a variety of inflammatory and surgical conditions.[28,29]

In the present study, we retrospectively investigated the correlations between various clinical variables, the preoperative NLR, and the incidence of severe postoperative complications in UC patients who had undergone emergency surgery and the factors that may predict the incidence of severe postoperative complications.

Methods

Patients

We retrospectively collected and reviewed the patient characteristics and perioperative data after obtaining approval from our institutional review board. A total of 105 patients who underwent emergency surgery or semi-emergency surgery for severe UC at the Department of Surgical Oncology, Osaka City University Hospital between January 1995 and December 2015 were included in this study. All the patients underwent total colectomy with ileostomy. All blood samples were obtained within 3 days before surgery.

Mortality was defined as death within 30 days of surgery or death that was directly related to the surgical procedure. Morbidity was defined as unexpected medical events within 30 days of the operation. The severity of complications was determined using the Clavien-Dindo Classification (CD) of Surgical Complications system.[30] In the case of patients who experienced more than 1 postoperative complication, the classification of the most severe complication was assigned. We defined complications of CD IIIb or higher as severe postoperative complication.

Variables

The following 23 parameters were evaluated as potential risk factors for postoperative complications: age at the time of surgery (≥ 70 or <70 years); sex; body mass index (BMI: ≥ 25 or <25 kg/m^2); timing of surgery; presence of massive hemorrhage,

Table 1 Clinical and disease characteristics in 105 patients who underwent emergency surgery for severe UC

Median age (yr; range)	49 (16–86)
Sex	
Male versus female	54 versus 51
BMI (kg/m^2)	
<25 versus ≥25	94 versus 11
Timing of surgery	
Semi-emergency versus emergency	51 versus 54
Surgical indication	
Massive hemorrhage versus toxic megacolon versus perforation versus refractory to medical treatment	20 versus 23 versus 10 versus 52
ASA score	
<3 versus ≥3	76 versus 29
Ischemic heart disease	
Absent versus present	94 versus 11
Chronic renal failure	
Absent versus present	102 versus 3
Chronic obstructive pulmonary disease	
Absent versus present	102 versus 3
Diabetes mellitus	
Absent versus present	91 versus 14
Operation time (min)	
<210 versus ≥210	48 versus 57
Intraoperative blood loss	
<180 versus ≥180	54 versus 51
Transfusion	
Absent versus present	68 versus 37
Preoperative serum CRP level (mg/dL)	
<3 versus ≥3	57 versus 48
Preoperative serum albumin level (g/dL)	
<2.5 versus ≥2.5	39 versus 66
Preoperative WBC (/mL)	
<10,000 versus ≥10,000	58 versus 47
Preoperative hemoglobin	
<10 versus ≥10	51 versus 54
Preoperative NLR	
<7 versus ≥7	55 versus 50
Anti-TNFα antibody administration	
Absent versus present	97 versus 8
Prednisolone administration	
None versus <20 mg versus ≥20 mg	16 versus 10 versus 79
Immunomodulators administration	
Absent versus present	80 versus 25

Table 2 Incidence of postoperative complications stratified according to the Clavien-Dindo classification

Postoperative complication (Clavien-Dindo classification)	Number of patients	Percentage
None	50	52.4
I	3	2.9
II	4	3.8
IIIa	31	29.5
IIIb	9	8.6
IV	6	5.7
V	2	1.9

The cutoff levels for patient age, operative time, amount of intraoperative blood loss, preoperative serum CRP, serum albumin levels, and serum total lymphocyte count were determined as mean values. The mean BMI value in the present series was extremely low (20.2 kg/m^2). In general, a BMI of ≥25 kg/m^2 is considered to reflect obesity in Japanese patients[31]; thus, the cutoff value for BMI was set at 25 kg/m^2. The cutoff value for NLR was determined to be 7 based on the receiver operating characteristic curve.

Statistical analysis

All statistical analyses were performed using the JMP 10 software program (SAS Institute Japan, Tokyo, Japan). The univariate analyses were performed using the χ^2 test or Fisher's exact test. All variables with $P < 0.05$ in the univariate analyses were included in a multivariate logistic regression analysis. $P < 0.05$ was considered to indicate statistical significance.

Results

Patient characteristics

The clinical characteristics of the 105 patients are summarized in Table 1. The mean age at surgery was 49 years (range, 16–86 years). Fifty-four of these patients (51.4%) underwent emergency surgery, whereas the other 48.6% patients underwent semi-emergency surgery. The most common indication was a treatment-refractory status followed by toxic megacolon and massive hemorrhage. Anti-TNFα antibodies were administered to 8 of the 105 (7.6%) patients. Immunomodulators were administered to 25 of the 105 patients (23.8%).

The postoperative complications are summarized in Table 2. In total, 17 (16.2%) UC patients had a severe postoperative complication CD ≥IIIb. Two patients died within 30 days after surgery. There

toxic megacolon, and bowel perforation; ASA score; presence of comorbidities (ischemic heart disease, chronic renal failure, chronic obstructive pulmonary disease, and diabetes mellitus); operative time (≥200 or <200 minutes); amount of blood loss (≥180 or <180 mL); use of perioperative transfusions; preoperative serum CRP level (≥3.0 or <3.0 g/mL); preoperative hemoglobin level (≥10 or <10 g/dL), preoperative serum albumin level (≥2.5 or <2.5 g/mL); preoperative NLR (≥7 or <7); and preoperative administration of steroids, TNFα antibodies, and/or immunomodulators within 1 month before surgery.

Table 3 Incidence of severe postoperative complications

Postoperative complication	Number of patients
Sepsis	6
Peritonitis, intra-abdominal abscess	
Pneumonia	4
Single or multiple organ failure	3
Death	2

were 6 cases of sepsis, 4 cases of peritonitis and/or intra-abdominal abscess, 4 cases of pneumonia, and 3 cases of organ failure (Table 3).

The results of the univariate analyses of the risk factors potentially associated with severe postoperative complications are shown in Table 4. Seven factors (timing of surgery, presence of toxic megacolon, presence of bowel perforation, ASA score of ≥ 3, preoperative serum WBC count of $\geq 10,000/$ mm^3, preoperative hemoglobin ≤ 10 g/dL, and NLR of $\geq$) were found to be significantly correlated with severe surgical complications.

Meanwhile, multivariate analyses revealed the ASA score, toxic megacolon, and NLR to be independent risk factors for severe postoperative complications. The preoperative administration of anti-TNFα antibodies or immunomodulators was not found to be a significant factor for severe complications. We classified the patients using the 3 above-noted independent risk factors and categorized them into 2 groups: patients with 2 to 3 risk factors were classified into the high-risk group (n = 41) and patients with 0 to 1 risk factors were classified into the low-risk group (n = 64). As a result, the frequency of severe postoperative complications was 34.1% (14 of 41) in the high-risk group, which was significantly ($P = 0.0001$) higher than that in the low-risk group (Table 5).

Discussion

Although the development of biological agents has led to new therapeutic options in recent years, surgery continues to play an important role in the therapeutic alternative approach in severe UC.[1] It is important to determine the disease activity early because this will significantly reduce delays in surgery, mortality, and morbidity in patients with serious UC. As for the index to evaluate disease severity, the Truelove and Witts' classification, which is based on various clinical parameters and laboratory findings (number of bowel movements; sedimentation rate; and the presence of tachycardia,

anemia, and fever) is one of the most widely used indices in clinical practice.[32] However, the complexity in the classification of some patients into the appropriate disease category and the changes in disease activity over time are major disadvantages of this index. Although the examination of endoscopically obtained biopsy specimens seems to be the most reliable method for estimating disease severity, such methods are invasive and costly.[33,34] Thus, there is a need for simple noninvasive methods and reliable markers that can be used to predict the patients who require emergency surgery for severe UC.

Noninvasive inflammation markers, such as CRP, WBC, and ESR, are widely acknowledged as important in the precise monitoring of disease activity.[14,15] Nevertheless, no optimal markers have been developed. Thus, the adjunctive use of additional serum markers may be of significant advantage in accuracy detecting the disease severity and predicting the patients who require surgery at an earlier time.

The NLR is one such inflammation marker. It is also a simple index that is calculated using only 2 parameters: total neutrophil and lymphocyte counts.[16] Because both factors are usually examined in daily clinical practice, the NLR is thought to be useful and convenient for detecting the inflammation status. We can obtain information about 2 different immune pathways from the NLR: neutrophils are responsible for lasting inflammation, whereas lymphocytes demonstrate the regulatory pathway.[16] Recently, Torun *et al*[25] and Acarturk *et al*[27] reported that the NLR is significantly higher in patients with active UC than that in UC patients who are in remission and that it is more sensitive than other markers of inflammation (WBC, CRP, ESR, and fibrinogen) in the detection of disease severity. Moreover, it has been shown that NLR is superior to WBC in the prediction of adverse outcomes in a variety of inflammatory and surgical conditions, such as pancreatitis, appendicitis, major vascular surgery, and critical care illness.[21–24]

Although the identification of risk factors for severe postoperative complications in patients with UC remains controversial, older age,[35,36] the presence of toxic megacolon, leukocytosis, anemia,[37,38] and the preoperative administration of steroids, thiopurine, immunomodulators, or anti-TNFα antibodies[39–41] have previously been reported as potential risk factors.

Table 4 Correlation between the various clinical factors and the incidence of severe postoperative complications

	Total no. of patients (n = 105)	No. of patients with CD IIIb or more severe postoperative complication (n = 17)	Univariate analysis P value	Multivariate analysis		
				OR	95% CI	P value
Age (yr)						
≥70	24	5	0.69			
<70	81	12				
Sex						
Male	54	11	0.35			
Female	51	6				
BMI (kg/m^2)						
≥25	11	3	0.38			
<25	94	14				
Timing of surgery						
Emergency	54	14	0.005	1.66	0.19–18.4	0.65
Semi-emergency	51	3				
Massive hemorrhage						
Present	20	2	0.51			
Absent	85	15				
Toxic megacolon						
Present	23	12	<0.0001	7.64	1.70–34.4	0.008
Absent	82	5				
Perforation						
Present	10	5	0.009	3.17	0.40–66.5	0.21
Absent	95	12				
ASA score						
≥3	29	11	0.0005	7.05	1.45–34.3	0.016
<3	76	6				
Ischemic heart disease						
Present	11	4	0.06			
Absent	94	13				
Chronic renal failure						
Present	3	3	NA			
Absent	102	14				
Chronic obstructive pulmonary disease						
Present	3	2	NA			
Absent	102	15				
Diabetes mellitus						
Present	14	2	0.82			
Absent	91	15				
Operation time (min)						
≥200	57	9	0.9			
<200	48	8				
Intraoperative blood loss						
≥180	52	13	0.03			
<180	53	4				
Transfusion						
Present	37	10	0.31			
Absent	68	7				
Preoperative serum WBC (/mm^3)						
≥10,000	47	13	0.009	4.02	0.82–88.7	0.07
<10,000	58	4				
Preoperative hemoglobin (g/dL)						
≥10	54	4	0.02	5.05	0.61–109.4	0.14
<10	51	13				
Preoperative serum CRP level (mg/dL)						
≥3	48	9	0.57			
<3	57	8				
Preoperative serum albumin level (g/dL)						
≥2.5	66	8	0.49			
<2.5	39	9				

Table 4   Continued

	Total no. of patients (n = 105)	No. of patients with CD IIIb or more severe postoperative complication (n = 17)	Univariate analysis P value	Multivariate analysis		
				OR	95% CI	P value
NLR						
≥7	50	15	0.0004	5.74	1.10–54.9	0.037
<7	55	2				
Prednisolone administration						
≥20 mg	79	11	0.76			
>20 mg	10	2				
None	16	4				
Anti-TNFα antibody administration						
Present	8	0	NA			
Absent	97	17				
Immunomodulator administration						
Present	25	1	NA			
Absent	80	16				

CI, confidence interval; OR, odds ratio.

It is well known that the prognosis of elderly UC patients undergoing emergency surgery is poor. However, the age of patients was not significantly associated with the frequency of postoperative complications in our study. When elderly UC patients are admitted to our hospital, physicians and surgeons collaborate at the time of admission to decide the necessity of emergency surgery within 7 days after admission. These early decisions about emergency surgery may reduce the incidence of severe postoperative complications.

Leukocytosis and anemia were also found to be significant risk factors for severe postoperative complications in the univariate analyses in the present study: however, these factors were not identified as independent factors in the multivariate analyses.

With regard to the correlation between the incidence of severe postoperative complications and the preoperative medical therapies, including steroids, anti-TNFα agents, and immunomodulators, it has been reported that the incidence of postoperative complications tends to be higher among patients who receive these drugs in preoperatively period.[39–41] However, several recent studies have reported that the use of these agents is not associated with higher rates of postoperative complications in patients with UC.[42,43] In the present study, only 8 patients received anti-TNFα antibodies in the preoperative period; thus, these factors were excluded from the statistical analysis. Although the association between the occurrence of postoperative complications and the preoperative administration of steroids and immunosuppressive agents remains controversial, the present study did not find that the use of either steroids or immunomodulators was a risk factor for severe postoperative complications.

In the present study, NLR of ≥7 was found to be an independent predictor of severe postoperative complications along with the presence of toxic megacolon and ASA score of ≥3. The delay in surgery is strongly corrected with mortality and morbidity in the patients with such high-risk factors. Therefore, emergency surgery should be performed promptly and carefully, and intensive postoperative care is needed in patients with high NLR.

This study is limited by its retrospective design and small numbers. Therefore, it is unclear whether the results can be extrapolated to the entire population of patients with severe acute UC. Furthermore, many of the patients were referred to our center after having been hospitalized elsewhere, with no records of IAP measurements.

Table 5   Correlation between the incidence of severe postoperative complications subdivided by the number of risk factors

Number of risk factors	Number of all patients	No. of patients with CD IIIb or more severe postoperative complication	P value
2 or 3	41	14	0.0001
0 or 1	64	3	

Conclusions

In this retrospective study, the presence of toxic megacolon, ASA score of ≥ 3, and NLR of ≥ 7 were found to be significantly associated with the incidence of severe postoperative complications in patients who underwent emergency surgery for UC. This was a single-arm retrospective study; thus, further large prospective studies are required to confirm the present findings.

References

1. Kornbluth A, Sachar DB. Practice parameters of the Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults. *Am J Gastroenterol* 2010; **105**(5):501–523

2. Turner D, Walsh CM, Steinhart AH, Griffiths AM. Response to corticosteroids in severe ulcerative colitis: a systematic review of the literature and a meta-regression. *Clin Gastroenterol Hepatol* 2007;**5**(1):103–110

3. Van Assche G, Vermeire S, Rutgeerts P. Management of acute severe colitis. *Gut* 2011;**60**(1):130–133

4. Hare NC, Amott ID, Satsangi J. Therapeutic options in acute severe ulcerative colitis. *Expert Rev Gastroenterol Hepatol* 2008; **2**(3):357–370

5. Jamerot G, Hertervig E, Fins-Liby I, Blomquist L, Grano C, Vilen M *et al*. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. *Gastroenterology* 2005;**128**(7):1805–1811

6. Aratari A, Papi C, Clemente V, Moretti A, Luchetti R, Koch M *et al*. Colectomy rate in acute severe ulcerative colitis in the infliximab era. *Digest Liver Dis* 2008;**40**(10):2008

7. ZampelColombel JF, Rutgeerts P, Reinisch W, Esser D, Wang Y, Lang Y *et al*. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. *Gastroenterology* 2011;**141**(4):1194–1201

8. Mowat C, Cole A, Windsor A, Ahmad T, Amott I, Driscoll R *et al*. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011;**60**(5):571–607

9. de Silva S, Ma C, Proulx MC, Crespin M, Kaplan BS, Hubbard J *et al*. Postoperative complications and mortality following colectomy for ulcerative colitis. *Clin Gastroenterol Hepatol* 2011; **9**(11):972–980

10. Miki C, Ohmori Y, Yoshiyama S, Toiyama Y, Araki T, Uchida K *et al*. Factors predicting postoperative infectious complications and early induction of inflammatory mediators in ulcerative colitis patients. *World J Surg* 2007;**31**(3):522–529

11. Alves A, Pants Y, Bouhnk Y, Maylin V, Lavergne-Slove A, Valleur P. Subtotal colectomy for severe acute colitis: a 20-year experience of a tertiary care center with aggressive and early surgical policy. *J Am Coll Surg* 2003;**197**(3):379–385

12. Ma C, Crespin M, Proulx MC, de Silva S, Crespin M, Hubbard J *et al*. Postoperative complications following colectomy for ulcerative colitis: a validation study. *BMC Gastroenterol* 2012; **12**(1):39–48

13. Randall J, Singh B, Warren BF, Travis SPL, Mortensen NJ, Geroge BD. Delayed surgery for acute severe colitis is associated with increased risk of postoperative complications. *Br J Surg* 2010;**97**(3):404–409

14. Sandborn WJ, Loftus EV Jr, Colombel JF, Seibold F, Homburger HA, Sedid B *et al*. Evaluation of serologic disease markers in a population-based cohort of patients with ulcerative colitis and Crohn's disease. *Inflamm Bowel Dis* 2001;**7**(3):192–201

15. Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? *Gut* 2006;**55**(3):426–431

16. Zahorec R. Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy* 2001;**102**(1):5–14

17. Maeda K, Shibutani M, Otani H, Nagahara H, Sugano K, Ikeya T *et al*. Prognostic value of preoperative inflammation-based prognostic scores in patients with stage IV colorectal cancer who undergo palliative resection of asymptomatic primary tumors. *Anticancer Res* 2013;**33**(12):5567–5574

18. Garcea G, Ladwa N, Metcalfe MS, Dennison AR, Berry DP. Preoperative neutrophil-to-lymphocyte ratio (NLR) is associated with reduced disease-free survival following curative resection of pancreatic adenocarcinoma. *World J Surg* 2011; **35**(4):868–872

19. Yamanaka T, Matsumoto S, Teramukai S, Ishikawa R, Nagai Y, Fukushima M. The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. *Oncology* 2007;**73**(3-4):215–220

20. Kim HS, Han KH, Chung HH, Kim JW, Park NH, Song YS *et al*. Neutrophil to lymphocyte ratio for preoperative diagnosis of uterine sarcomas: a case-matched comparison. *Eur J Sur Oncol* 2010:**36**(7):691–698

21. Lee SK, Lee SC, Park JW, Lee SK, Kim SJ. The utility of the preoperative neutrophil-to-lymphocyte ratio in predicting severe cholecystitis. *BMC Surg* 2014; DOI: 10.1186/ 1471-2482-14-100

22. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg* 2012;**97**(4):299–304

23. Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervaention. *Am J Cardiol* 2006;**97**(7):993–996

24. Tamhane UU, Aneja S, Montogomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol* 2008;**102**(6):653–657

25. Torun S, Tune BD, Suvak B, Sayilir A, Ozderin YO, Beyazit Y, Kayacetin E. Assessment of neutrophil-lymphocyte ratio in ulcerative colitis: a promising marker in predicting disease severity. *Clin Res Haptol Gastroenterol* 2012;**36**(5):491–497

26. Celikbilek, M, Dogan S, Ozbakir O, Zararsiz G, Kucuk H, Grusoy S *et al*. Neutrophil-lymphocyte ratio as a predictor of disease severity in ulcerative colitis. *J Clin Lab Anal* 2013;**27**(1):72–76

27. Acarturk G, Acay A, Denir K, Ulu MS, Ahsen A, Yuksel S. Neutrophil-to-lymphocyte ratio in inflammatory bowel dis-ease-as a new predictor of disease severity. *Bratisl Lek Listy* 2015;**116**(4):213–217

28. Cook EJ, Walsh SR, Farooq N, Alberts JC, Justin TA, Keeling NJ. Post-operative neutrophil-lymphocyte ratio predicts com-plications following colorectal surgery. *Int J Surg* 2007;**5**(1):27–30

29. Forget P, Dinant V, de Kock M. Is the neutrophil-to-lymphocyte ratio more correlated than C-reactive protein with postoperative complications after major abdominal surgery? *PEER J* 2015; DOI: 10.7717/peerj.713

30. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;**240**(2):205–213

31. The Examination Committee of Criteria for 'Obesity Disease' in Japan, Japan Society for the Study of Obesity. New criteria for 'obesity disease' in Japan. *Circ J* 2002;**66**(11):987–992

32. Truelove SC, Witts LJ. Corticosone in ulcerative colitis; final report on a therapeutic trial. *BMJ* 1955;**2**(4947):1041–1048

33. Allez M, Lemann M. Role of endoscopy in predicting the disease course in inflammatory bowel disease. *World J Gastro-enterol* 2010;**16**(21):2626–2632

34. Travis SPL, Schnell D, Krezeski P, Abereu MT, Altman DG, Colombel JF *et al*. Reliability and initial validation of the ulcerative colitis endoscopic index of severity. *Gastroenterology* 2013;**145**(5):987–995

35. Ikeuchi H, Uchino M, Matsuoka H, Bando T, Hirata A, Takesue Y *et al*. Prognosis following emergency surgery for ulcerative colitis in elderly patients. *Surg Today* 2014;**44**(1):39–43

36. Ananthakrishnan AN, McGinley EL, Binion DG. Inflammato-ry bowel disease in the elderly is associated with worse outcomes: a national study of hospitalizations. *Inflamm Bowel Dis* 2009;**15**(2):182–189

37. Uchino M, Ikeuchi H, Tsuchida T, Nakajima K, Tomita N, Takesue Y. Surgical site infection following surgery for inflammatory bowel disease in patients with clean-contami-nated wounds. *World J Surg* 2009;**33**(5):1042–1048

38. Araki T, Okita Y, Uchino M, Ikeuchi H, Sasaki I, Funayana Y *et al*. Risk factors for surgical site infection in Japanese patients with ulcerative colitis: multicenter prospective study. *Surg Today* 2014;**44**(6):1072–1078

39. Subramanian V, Saxena S, Kang JY, Pollok RCG. Preoperative steroid use and risk of postoperative complications in patients with inflammatory bowel disease undergoing abdominal surgery. *Am J Gastroenterol* 2008;**103**(9):2373–2381

40. Ferrante M, D'Hoore A, Vermeire S, Declerk D, Noman M, Van Assche G *et al*. Corticosteroids but not infliximab increase short-term postoperative infectious complications in patients with ulcerative colitis. *Inflamm Bowel Dis* 2009;**15**(7):1062–1070

41. Schluenders SJ, Ippoliti A, Dubinsky M, Vasiliauskas EA, Mei L, Targan SR *et al*. Does infliximab influence surgical morbidity of ileal pouch-anal anastomosis in patients with ulcerative colitis? *Dis Clon Rectum* 2007;**50**(11):1747–1753

42. Ali T, Yun L, Rubin D. Risk of post-operative complications associated with anti-TNF therapy in inflammatory bowel disease. *World J Gastroenterol* 2012;**18**(3):197–204

43. Nguyen GC, Elnahas A, Jackson TD. The impact of preoper-ative steroid use on short-term outcomes following surgery for inflammatory bowel disease. *J Crohn's Colitis* 2014;**8**(12):1661–1667