Journal of Gastrointestinal Surgery (2018) 22:1593–1602
https://doi.org/10.1007/s11605-018-3786-x

ORIGINAL ARTICLE

Toward a More Sensitive Endpoint for Assessing Postoperative Complications in Patients with Inflammatory Bowel Disease: a Comparison Between Comprehensive Complication Index (CCI) and Clavien-Dindo Classification (CDC)

Feng Zhu[1] · Dengyu Feng[2] · Tenghui Zhang[2] · Lili Gu[2] · Weiming Zhu[2] · Zhen Guo[2] · Yi Li[2] · Jianfeng Gong[1,2] · Ning Li[2] · Jieshou Li[2]

Received: 2 March 2018 / Accepted: 13 April 2018 / Published online: 15 May 2018

Abstract

Background The comprehensive complication index (CCI) is a novel approach to evaluate complications. However, application of the CCI in inflammatory bowel disease (IBD) population is scarce and the difference between the CCI and the Clavien-Dindo classification (CDC) remains unknown. The aim of this study was to compare the CCI to the conventional CDC by applying the CCI among the IBD patients.

Methods The data of 426 IBD patients who underwent surgery between September 1, 2015 and August 31, 2017 were collected. Univariate and multivariate analyses were conducted to identify risk factors for postoperative complications. The efficacy of CCI and CDC was compared using correlation analysis and logistic regression. Cumulative sum control (CUSUM) models were applied to monitor the CCI continuously.

Results Totally, 297 complications occurred in 144 (33.8%) patients. The rate of severe complications (CDC grade ≥ III) was 12.9% and the mean CCI was 9.8 ± 15.5. Preoperative glucocorticoids usage and previous abdominal surgery were related to higher CCI value ($p = 0.002$, $p = 0.006$, respectively) but not related to higher incidence of severe complications (CDC grade ≥ III) ($p = 0.117$, $p = 0.177$, respectively). In patients with multiple complications, the CCI demonstrated a stronger correlation with hospital stay ($\rho = 0.604$, $p < 0.001$) than CDC ($\rho = 0.508$, $p < 0.001$). Higher CCI value ($p < 0.001$, OR 1.161, 95% CI 1.093–1.234) and the CDC grade ($p < 0.001$, OR 3.811, 95% CI 2.283–6.362) were risk factors for prolonged LOS. In the CUSUM-CCI model of IBD surgery, a gradual decrease was observed over time.

Conclusions The CCI and the CDC are both risk factors for prolonged postoperative LOS after surgery for IBD patients. The CCI is more strongly correlated with postoperative LOS than is the conventional CDC. The CUSUM-CCI model is effective in monitoring surgical quality.

Keywords Comprehensive complication index · Postoperative morbidity · Surgical quality monitoring

Feng Zhu and Dengyu Feng are first co-author

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11605-018-3786-x) contains supplementary material, which is available to authorized users.

✉ Jianfeng Gong
gongjianfeng@aliyun.com

[1] Department of General Surgery, Jinling Hospital, Nanjing Medical University, East Zhongshan Road, 305, Nanjing 210002, China

[2] Department of General Surgery, Jinling Hospital, Medical School of Nanjing University, East Zhongshan Road, 305, Nanjing 210002, China

Abbreviations

CD	Crohn's disease
UC	Ulcerative colitis
IBD	Inflammatory bowel disease
CCI	Comprehensive complication index
CDC	Clavien-Dindo classification

Introduction

Surgery remains an important approach to treat inflammatory bowel disease (IBD) despite the great advances in surgical

techniques and postoperative care. Roughly, 80% of Crohn's disease (CD) patients and 20% of ulcerative colitis (UC) patients will require surgical intervention in their lifetime.[1–3] The surgical technique has significantly evolved over the last two decades,[4] shifting the focus from mortality toward other endpoints such as morbidity, quality of life, and medical costs. Therefore, it is important to find an objective and reproducible tool to achieve quality control and to assess the postoperative morbidity.

Currently, the most commonly used grading system of postoperative complications is the Clavien-Dindo classification (CDC) first described in 2004[5] and reassessed in 2009.[6] This system was designed to capture postoperative complications in five ranks according to the invasiveness of the treatment required.[5,6] It is widely used for its reproducible interpretation of postoperative complications.[7–9] However, about 80% of the literature describing complications failed to provide information about their severity[10] because the CDC system only reports the highest grade of complication in most studies, thereby underestimating the disease burden in many cases.

The comprehensive complication index (CCI) is a newly developed approach adopting methods from operation-risk-index analysis in marketing research, which takes all postoperative experience into considerations.[11] Based on the CDC system, the CCI uses a mathematical formula to integrate all complications graded in CDC system, summarizing the postoperative course with a new scale ranging from 0 (no complication) to 100 (death). For example, if one patient developed postoperative anastomotic leak requiring drainage, this patient is considered to have grade IIIa complication according to CDC and the corresponding CCI value is 26.2. The CCI has already been proven to be a more sensitive endpoint to detect differences of treatment effect in three randomized trials.[12] Another recent study revealed CCI is more strongly related to postoperative hospital stay than CDC in gastric cancer surgery.[13]

Up to 21% of CD patients and 9–65% UC patients who underwent surgery develop early postoperative complications.[14,15] Also, postoperative morbidity is significantly higher after IBD surgery compared to other colorectal procedures due to malnutrition, hypoalbuminemia, preoperative inflammatory status, previous laparotomy, prolonged glucocorticoid, and biologics usage.[16,17] More importantly, it is common for IBD patient to develop multiple complications.[18,19] The application of CCI in patients undergoing colectomy has been described in UC patients,[20,21] however, the comparison of it with CDC system in IBD surgery is lacking. Therefore, we hypothesized that the CCI system was more applicable in IBD patients undergoing surgery than the CDC system. The aim of this study was to compare the CCI with the conventional CDC at our IBD center and longitudinally monitor complications using the CCI system.

Methods

Patients

The protocol of this study was approved by the Ethics Committee of Jinling Hospital. Consecutive patients who underwent surgery in Jinling Hospital from Sep 1, 2015 to Aug 31, 2017 for IBD were screened from the prospectively maintained IBD database. Any bowel resection or strictureplasty were included and abscess drainage without bowel resection, reversal of ileostomy or colostomy, bypass surgery, reoperation for postoperative complications, as well as those who underwent surgery for isolated perianal CD lesions were excluded from the study. Details of surgical technique were described as previously.[22]

Demographic data of gender, age, age at diagnosis, body mass index (BMI), diagnosis, operation method (open, laparoscopic), surgical procedure (small bowel resection, ileocecal/right colectomy, transverse colectomy, left colectomy, sigmoid/rectal resection, (sub) total colectomy), emergent procedure (yes/no), disease phenotype and behavior at time of surgery (Montreal classification),[23] history of previous abdominal surgery, intraoperative parameters including duration of surgery (in minutes), and estimated blood loss (in mL) were reviewed. Preoperative 5-ASA, immunomodulators and steroids usage was defined as 5-ASA, azathioprine, 6-mercaptopurine and corticosteroids within 4 weeks before surgery. Preoperative biologics usage was defined as infliximab administered within 12 weeks prior to surgery. Inpatient records were reviewed for total medical cost and postoperative length of stay (LOS). Comorbidity data were collected and converted to Charlson comorbidity index, which is the most widely used scale to quantify the overall burden of comorbidities.[24] Total medical cost was collected from the nursing records. Briefly, total medical cost included expenditures for medication, operation, examination, laboratory tests, and use of consumptive material. Missing or incomplete data were collected by reviewing medical records from the hospital and noted accordingly in the results if unavailable.

Postoperative Management

An enhanced recovery after surgery (ERAS) protocol was applied. Briefly, early enteral nutrition was started from postoperative day (POD) 0 and adjusted depending on the patient's physical status and type of surgery. Daily volume and speed were added until full capacity if the patient displayed no signs of intolerance such as abdominal distension. Urinary catheter was removed on POD 1. Postoperative pain control was performed using patient-controlled analgesia comprising sufentanil for maximally 48 h. A semi-fluid diet was added followed by a semi-blended diet according to patients' tolerance. Serum laboratory tests were scheduled as clinically

needed including erythrocyte count, white blood cell count, platelet count, hemoglobin concentration, neutrophil to lymphocyte ratio, electrolytes, albumin, C-reactive protein (CRP), interlukin-6 (IL-6), and procalcitonin (PCT) level.

Criteria for Discharge

The attending surgeon reviewed laboratory tests and vital signs were measured on a daily base. Discharge was postponed for patients who had elevated body temperature (> 37.8 °C). In the absence of complications, patients were discharged provided that they tolerated a regular diet or full dosage of enteral nutrition, had passed stool, weaned off intravenous fluids, and were fully ambulant with oral analgesics.

Complications

Complication data were extracted from the database where detailed clinical course and events were described according to daily ward rounds. Clinical events were converted to the CDC grade with delicate interpretation of the five special clinical scenarios described by Clavien et al.[25] For example, intra-abdominal abscess treated with both antibiotics and subsequent drainage was counted as separate complications. Postoperative ileus requiring kinetics, fever ≥ 38.5 °C treated with antipyretics, postoperative retention of urine treated with diuretics, electrolyte disturbance, and wound infection opened at beside were considered as grade I complications. Surgical site or remote infection treated with antibiotics, non-operated bowel obstruction, gastrointestinal hemorrhage treated with transfusion, deep vein thrombosis treated with anticoagulants, and anastomotic leakage treated with total parenteral nutrition for ≥2 weeks was considered as grade II complications. Intra-abdominal abscess or anastomotic leakage treated with percutaneous drainage, endoscopically treated gastrointestinal hemorrhage, wound dehiscence requiring re-suture, urinary retention, and intra-cavity fluid collection treated with percutaneous drainage was considered as grade IIIa complications. Anastomotic leakage, anastomotic stricture, stoma ischemia, stoma stricture, intra-abdominal abscess re-operated upon were considered as grade IIIb complications. Single- and multi-organ dysfunction were considered as grade IVa and IVb complications, respectively. Death was considered as grade V complication. Complications following the reoperation were integrated into the primary operation. All complications that occurred within 30 days after surgery or prior to discharge were considered relevant to the surgery.

Comprehensive Complication Index

The calculation of the CCI has been described previously in details by Slankamenac K et al.[11] Generally, this index integrates the perspective of patients and physicians by investigating the median reference value of patients (MRV_{pat}) and that of physicians (MRV_{phys}). After multiplication and summary of the MRVs, the square root of the raw CCI was divided by two.

$$CCI = \sqrt{\sum(MRVphys \times MRVpat)/2}$$

The calculator is accessible on https://www.assessurgery.com. For this study, the CDC complication data for each patient were calculated and the final CCI were acquired for analysis.

Continuous Monitoring for the Complication Index of Individual Surgeons

The cumulative summation (CUSUM) technique is a tool for performance monitoring in surgery.[26] The cumulative sum is $\sum_{i=1}^{n}(Xi-\mu)$, in which Xi represents the CCI for each operation and μ is the target value. This method continuously calculates the accumulated difference between the event and target value. Implementation of the CCI in CUSUM model provides delicate visualization of surgical quality which would otherwise be crude in the scale of the CDC. Previous study has described this method in gastric cancer.[13] In our center, surgeries for CD were performed by surgeon A while surgeries for UC were performed by surgeon B. The case-event CUSUM chart of the second year was drawn for surgeon A and B with the target value set for the average CCI of the first year (8.5 vs. 16.9).

Statistics

Data for demographic characteristics were expressed as mean ± SD or median (range). Kolmogorov-Smirnov method was used to test the normality of the variables. Continuous variables were analyzed using Student t test or Mann-Whitney U test as appropriate. Categorical variables were compared using χ^2 test.

Univariate analysis was conducted to detect any risk factors of developing postoperative complications. Significant factors were further analyzed for between-group difference of the CCI value and the CDC grade using χ^2 test. Spearman's rank test was performed to compare the correlation of each complication scale with postoperative LOS and medical cost. Correlation coefficients were calculated for comparison and scatterplots were drawn. Univariate analysis was performed to compare difference of prolonged LOS in various factors. Significant factors were assembled for binary logistic regression model with each complication system. Receiver operating characteristic curve analysis was conducted to investigate the relationship between the CCI and prolonged LOS.

Statistical Package for Social Science version 20.0 (SPSS, Chicago, IL, USA) was used for all analyses. A two-sided p value of < 0.05 were considered as statistically significant.

Results

Patient Characteristics

Five hundred and seventy-five patients who underwent surgery for IBD from September 2015 to August 2017 were screened. One hundred and forty-nine were excluded due to stoma closure ($n = 121$), bypass surgery ($n = 12$), reoperation for complications as initial surgery ($n = 9$), abscess drainage ($n = 5$), and surgery for isolated perianal disease ($n = 2$). Finally, 426 patients were enrolled in the study, including 331 CD and 95 UC patients.

Demographic and baseline characteristics were shown in Table 1. Age, gender, BMI, disease classification, and preoperative medication including 5-ASA, immunomodulators, biologics were similar between patients who developed postoperative complications and those did not. In contrast, ASA score, Charlson comorbidity index, preoperative glucocorticoids usage showed significant difference between groups. Preoperative serum albumin level was lower (34.8 ± 5.8 vs. 38.2 ± 4.4 g/L) and serum CRP level was higher (30.9 ± 47.1 vs. 13.9 ± 27.0 mg/L) in patients with complications than those without. Complicated patients had longer postoperative LOS (19.7 ± 8.6 vs. 8.2 ± 3.3 d) and higher medical cost ($97{,}410 \pm 40{,}201$ vs. $56{,}183 \pm 22{,}297$ CNY) compared with non-complicated patients.

Perioperative parameters were shown in Table 2. There was no difference in operation method, operation time, estimated blood loss and intraoperative transfusion between the two groups. However, emergent procedure ($p < 0.001$) and (sub) total colectomy/IPAA ($p = 0.001$) were related to higher incidence of complications.

Complications

Totally, 297 complications occurred in 144 (33.8%) patients. The rate of severe complications (CDC grade ≥ III) was 12.9% and mean CCI was 9.7 ± 14.5. The overall complication rate was 28.1% for CD and 53.7% for UC, respectively. One hundred and three of the 144 patients developed multiple complications and 41 patients developed a single complication. According to the Clavien-Dindo classification, 18 patients had grade I complications, 69 patients had grade II complications, 40 patients had grade IIIa complications, 10 patients had grade IIIb complications, 5 patients had grade IVa complications, 1 patient had grade IVb complication and 1 patient died of pulmonary and renal failure after septic shock.

The most frequent complication was wound complications (13.1%), followed by ileus (12.0%), intra-abdominal abscess (7.7%), and urinary complications (6.8%). Eight patients underwent reoperation because of anastomotic leak (4/8), intra-abdominal sepsis (2/8), stricture of the stoma (1/8), and necrosis of the stoma (1/8). (For details of recorded complications, see Supplementary Table A and B).

The distribution of CCI and CDC was shown in Fig. 1. The most frequent CDC complications were grade II and IIIa. Similarly, the CCI value of most cases was in the range of 20.9–26.1 and 26.2–33.6, since 20.9 and 26.2 represented the CCI value of single grade II and IIIa Clavien-Dindo complication, respectively. In patients with complications, the mean CCI was 28.9 ± 12.8. The rate of severe complications (≥ III) was 39.5%, however, 81 (56.2%) cases demonstrated a CCI value of ≥ 26.2.

Comparison of CDC and CCI

Significant variables in the univariate analysis were further analyzed using χ^2 test or student t test to compare the sensitivity of CDC and CCI. The results were shown in Table 3. ASA score ≥ 3, preoperative hypoalbuminemia, elevated CRP level, emergent surgery, and total colectomy were related to higher incidence of severe complications and higher CCI value. Charlson score index, preoperative glucocorticoids usage, and previous abdominal surgery were not associated with higher incidence of severe complications ($p = 0.682$, $p = 0.117$, $p = 0.177$, respectively), however, they were associated with higher CCI value ($p = 0.009$, $p = 0.002$, $p = 0.006$, respectively).

Correlation Analysis

The capability of CDC and CCI to reflect postoperative morbidity was evaluated by their correlation with postoperative LOS as well as medical cost. Notably, in patients with multiple complications ($N = 103$), the CCI showed a stronger positive correlation ($\rho = 0.604$, $p < 0.001$) with postoperative LOS than CDC ($\rho = 0.508$, $p < 0.001$). Scatterplots and correlation coefficient were shown in Fig. 2. In patients with prolonged LOS (> 30 days, $N = 20$), the CCI displayed a significant correlation ($\rho = 0.481$, $p = 0.032$) with postoperative LOS while the CDC did not ($\rho = 0.342$, $p = 0.140$). Both CCI and CDC were correlated with medical cost ($\rho = 0.554$ vs. $\rho = 0.552$, $p < 0.001$ vs. $p < 0.001$).

Logistic Regression

Apart from the CCI value and CDC grade, univariate analysis showed preoperative glucocorticoids usage ($p = 0.050$) and CRP level > 8 mg/L ($p = 0.002$) were related to prolonged LOS. Multivariate logistic regression analysis was performed

Table 1 Patients' characteristics

	With complications ($n = 144$)	Without complications ($n = 282$)	P value
Age (year)	35.1 ± 11.7	33.2 ± 11.6	0.890[a]
Gender (male)	86	184	0.263[b]
Body mass index (kg/m^2)	18.5 ± 2.9	18.8 ± 2.8	0.089[a]
Disease classification			
CD[†]			
L1/L2/L3	10/26/52	28/75/96	0.472[b]
B1/B2/B3	3/53/32	3/119/89	0.592[c]
With perianal lesion	25	54	0.628[b]
UC[‡]			
E2/E3	22/23	19/26	0.525[b]
ASA score III-IV	21	16	0.002[b]
Charlson score			
0/1/2	97/33/14	232/38/12	0.002[b]
Preoperative Alb (g/L)[μ]	34.8	38.2	< 0.001[a]
Preoperative CRP (mg/L)[ν]	30.9	13.9	< 0.001[a]
Preoperative medication			
5-ASA	66	122	0.130[b]
Immunomodulators	61	108	0.082[b]
Glucocorticoids	62	83	0.005[b]
Biologics	9	15	0.504[b]
Previous laparotomy	42	47	0.003[b]

Data were calculated using [a] Student t test; [b] χ^2 test; [c] Fisher's exact test; and [d] Mann-Whitney U test

ASA American society of anesthesiologists; *CRP* C-reactive protein; *5-ASA* 5-aminosalicylic acid;

[†] Not determined in 44 CD patients

[‡] Not determined in 5 UC patients

[μ] Not recorded for 31 patients

[ν] Not recorded for 42 patients

and the results were summarized in Table 4. Neither preoperative glucocorticoids nor elevated CRP level could predict prolonged LOS. However, higher CCI value ($p < 0.001$, OR 1.161, 95% CI 1.093–1.234) and CDC grade ($p < 0.001$, OR 3.811, 95% CI 2.283–6.362) both conferred to an increased risk of prolonged LOS. Notably, the CCI model had a higher R^2 than the CDC model (0.568 vs. 0.467).

Monitoring the Complication Rate of Individual Surgeon

CCI-CUSUM charts were drawn to monitor postoperative complication outcome of each surgeon. Target value was set for the average CCI of the first year. For surgeon A, 331 cases were depicted with the target value set for 8.5. In Fig. 3a, the CUSUM score showed a constant fluctuation around base line during the first year, with the highest value (124.9) peaking at case 26. In the second year, the CUSUM score showed a gradual decrease with a final score of − 176.2 at case 331, indicating improvement of the complication outcome. For surgeon B, 95 cases were depicted with the target value set for 16.9. CUSUM score in Fig. 3b peaked at case 5 (61.0), followed by a gradual decrease. The final score was − 111.0, indicating improvement of the complication outcome.

Receiver Operating Characteristic Curve Analysis

Receiver operating characteristic curve analysis demonstrated that the CCI value is predictive of prolonged postoperative length of stay (> 30 days) with an optimal cutoff value of 24.2. The area under curve was 0.951 (95% CI 0.925 to 0.970, $p < 0.001$). The sensitivity was 94.1% and the specificity was 85.0%, respectively. (Fig. 4).

Table 2 Perioperative parameters and surgical procedure

	Complicated ($n = 144$)	Non-complicated ($n = 282$)	P value
Emergent procedure (n = 28)	19	9	<0.001[b]
Laparoscopic surgery ($n = 189$)	69	120	0.292[b]
Surgical procedure[†]			
Strictureplasty	2	7	
Small bowel resection	10	28	
Ileocecal/right colectomy	51	144	
Transverse colectomy	6	13	
Left/Sigmoid colectomy	22	40	
(Sub)total colectomy/IPAA	59	50	< 0.001[b]
Operation time (min)	168.8 ± 55.4	155.2 ± 60.7	0.062[a]
Estimated blood loss (mL)	150 (10–800)	145 (10–700)	0.291[d]
Intraoperative transfusion	37	56	0.270[b]
Postoperative LOS (day)	19.7 ± 8.6	8.2 ± 3.3	< 0.001[a]
Medical cost (CNY)	97,410 ± 40,201	56,183 ± 22,297	< 0.001[a]

Data were calculated using [a] Student t test, [b] χ^2 test, [c] Fisher's exact test, [d] Mann-Whitney U test

CNY, Chinese yuan; *LOS* length of stay; *IPAA*, ileal-pouch anal anastomosis

[†] Nine CD patients underwent subtotal colectomy and 5 CD patients underwent total colectomy. 4 patients underwent combined procedure of transverse colectomy and right colectomy. 2 patients underwent combined procedure of ileal strictureplasty and right colectomy

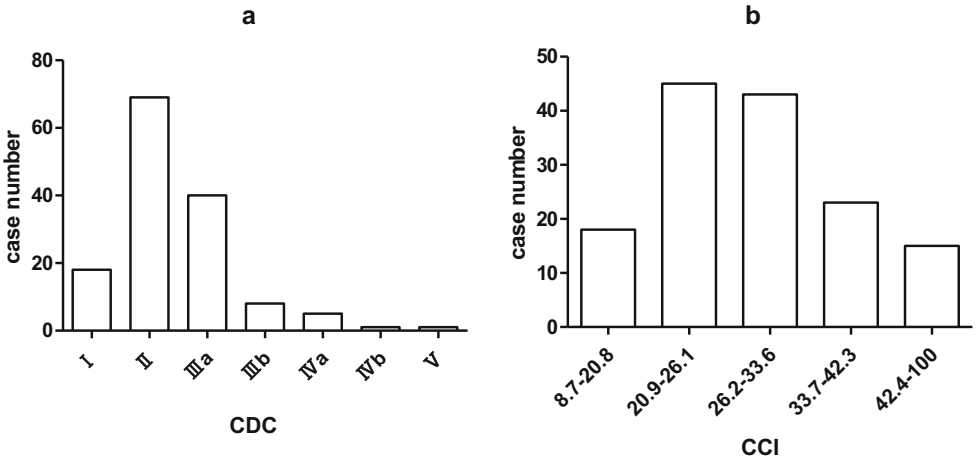

Fig. 1 Overall distribution of complication in different scales. Most cases were graded as II or IIIa according to CDC. Similarly, the CCI of most cases clustered in the values that represented CDC grade II and IIIa

Discussion

The complication rate after IBD surgery is higher than other intestinal diseases due to preoperative poor nutrition status, preoperative medication and inflammatory status.[14,17,27] To date, this is the first study comparing CCI and CDC system after IBD surgery. The results revealed that CCI had a better reflection of the postoperative morbidity in IBD patients who underwent surgery compared to the conventional CDC system. Our data revealed the CD and UC patients who underwent surgery had a mean CCI of 8.0 and 15.8, respectively. These results proved CCI as a qualified marker to reflect postoperative surgical morbidity in IBD patients.

Table 3 Comparison of the CCI and the CDC regarding factors significantly related with complication rate

Variables	No. of patients	CDC ≥ IIIa (%)	*P* value	Mean CCI (SD)	*P* value
ASA score					
≥ III	37	29.7		18.7 ± 21.8	
< III	389	12.1	0.003	8.9 ± 14.6	0.001
Charlson score					
0	329	13.4		8.2 ± 14.1	
1	71	12.7		14.1 ± 18.9	
2	26	19.2	0.682	17.2 ± 19.1	0.009[a]
Preoperative albumin level					
< 35 g/L	117	22.2		16.3 ± 16.8	
≥ 35 g/L	278	5.0	< 0.001	6.0 ± 12.8	< 0.001
Preoperative CRP					
> 8 mg/L	153	18.3		13.8 ± 17.1	
≤ 8 mg/L	231	4.8	< 0.001	5.6 ± 12.1	0.001
Preoperative glucocorticoid usage					
With	145	17.2		12.5 ± 17.6	
Without	281	11.7	0.117	8.3 ± 14.2	0.002
Emergent procedure					
Yes	28	28.6		19.6 ± 17.1	
No	398	12.6	0.017	9.1 ± 15.2	0.004
Previous laparotomy					
With	89	18.0		13.6 ± 18.3	
Without	337	12.5	0.177	8.7 ± 14.6	0.006

[a] Data were compared using ANOVA test

It is well known that the CDC focuses on the complication of highest grade while neglecting the concomitant ones. A significant proportion of IBD patients (71.5%) in this study developed two or more different complications. Therefore, failure to capture the number and the severity of minor complications will result in insufficient report of the postoperative morbidity in IBD patients. The CCI integrates all complications into one formula and depicts the entire spectrum of complications, thereby comprehensively demonstrating the postoperative morbidity. Additionally, comparison between multiple minor complications and single severe complication are often cumbersome under the CDC system. However, the CCI scale allows direct comparison of morbidity and identification of more severe patients, thus aiding in the clinical decision for IBD patients.

Due to its superiority, CCI instead of CDC has been used in many publications. For example, Kalisvaart et al.[28] reported liver transplantation had a median CCI of 37.1 at discharge and 47.6 after 6 months. Another study showed laparoscopic gastrectomy had a lower CCI of 4.9 vs. conventional open gastrectomy (9.0).[13] Kim et al. also revealed that CCI is more strongly correlated with postoperative hospital stay than is the conventional CDC after gastric cancer surgery. After externally analyzing the CCI value, Slankamenac et al.[12] found a more significant inter-group difference in postoperative morbidity with p value of 0.009 compared to the original study ($p = 0.035$).[29] Therefore, the CCI was able to compare morbidity after different surgery, to monitor the increase of disease burden over time, and was more sensitive to grade complications compared to the conventional grading system.

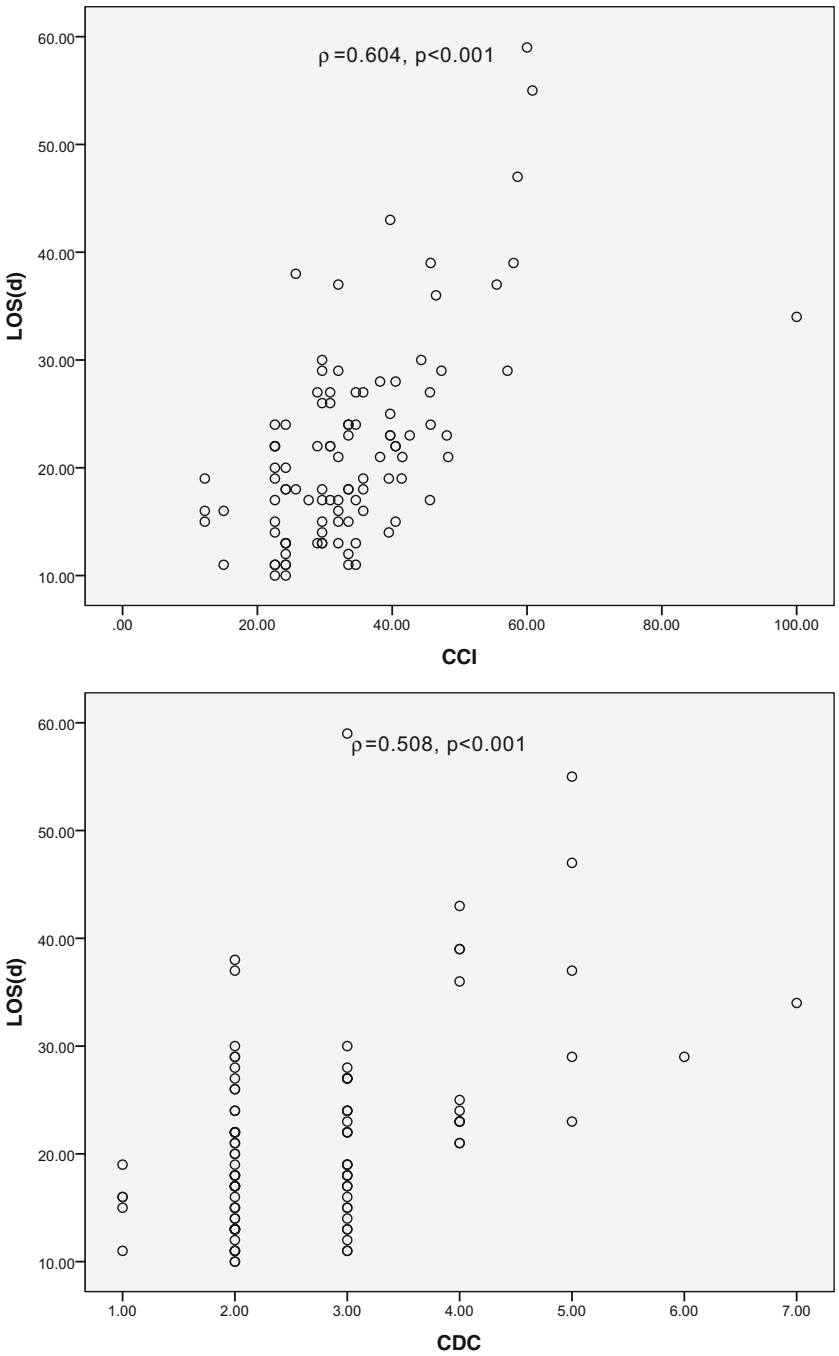

Fig. 2 Scatterplots demonstrating the relationship between each complication scale and LOS in patients with multiple complications. Spearman's rank test revealed the CCI had a stronger relationship with postoperative LOS than CDC ($\rho = 0.604$, $p < 0.001$ vs. $\rho = 0.508$, $p < 0.001$); LOS (d), length of stay (days)

In this study, patients with preoperative glucocorticoids usage had a higher CCI (12.5 vs. 8.3, $p = 0.002$) and a prolonged postoperative LOS ($p = 0.050$) according to univariate analysis. However, there was no difference of severe complications (CDC ≥ Gr III) in patients with preoperative glucocorticoids administration and those without (17.2 vs. 11.7%, $p = 0.117$). As indirect comparison of effect sizes, the between-group differences for the CCI presented lowest p value ($p = 0.002$), compared to the differences for the specific outcome "prolonged postoperative LOS" ($p = 0.050$) and the differences for the "rate of severe complication" according to CDC ($p = 0.117$). These findings suggest that the CCI has a higher sensitivity and may serve as a more effective endpoint for assessing clinical outcomes after IBD surgery.

Postoperative morbidity is measured in different ways. Medical cost and postoperative LOS are both good indicators of postoperative complications. However, the economic status of the patients and type of reimbursement in Chinese hospital may affect the medical cost to a great deal. On the contrary, our center had an established procedure for IBD patients and

Table 4 Logistic regression of factors associated with prolonged postoperative length of stay (LOS) (> 30 days)

Factors	β	Odds ratio	95% CI	P value	R^2
CCI model					0.568
CCI value	0.149	1.161	1.093–1.234	< 0.001	
CRP > 8 mg/L	0.699	2.012	0.472–8.577	0.345	
Preoperative glucocorticoids	0.741	2.097	0.584–7.534	0.256	
CDC model					0.467
CDC level	1.338	3.811	2.283–6.362	< 0.001	
CRP > 8 mg/L	1.199	3.315	0.864–12.724	0.081	
Preoperative glucocorticoids	1.031	2.803	0.851–9.236	0.090	

criteria for discharge. Therefore, our results showed that medical cost was only moderately related to the CCI value ($\rho = 0.554$, $p < 0.001$) while postoperative LOS was strongly related to the CCI value ($\rho = 0.756$, $p < 0.001$). In addition, after excluding patients with one or no complication, the correlation coefficient of CCI appeared significantly higher (0.604 vs. 0.508). In cases of prolonged hospital stay (> 30 days), CCI showed a significant correlation while CDC did not. This reflected the major drawback of reporting the most severe complication only in the CDC system and these results indicated that the CCI was more capable of grasping the magnitude and number of complications especially in multi-complicated patients.

The CCI value is a continuous scale ranging from 0 to 100 while most of the cases of our study clustered between 20.9 and 33.6. This is because the complications recorded in this study were primarily surgical site infection, which were treated with antibiotics or percutaneous drainage under local anesthesia. Ileus was another frequent complication but it was usually accompanied by complications of higher grades. Thus, complication grades that occurred most frequently were II and IIIa under the CDC system.

When the CCI and CDC were assembled for multivariate analysis, both complication scales were risk factors for prolonged LOS (> 30 days). However, the CCI model had a higher R^2 value. Since the R^2 value of each model

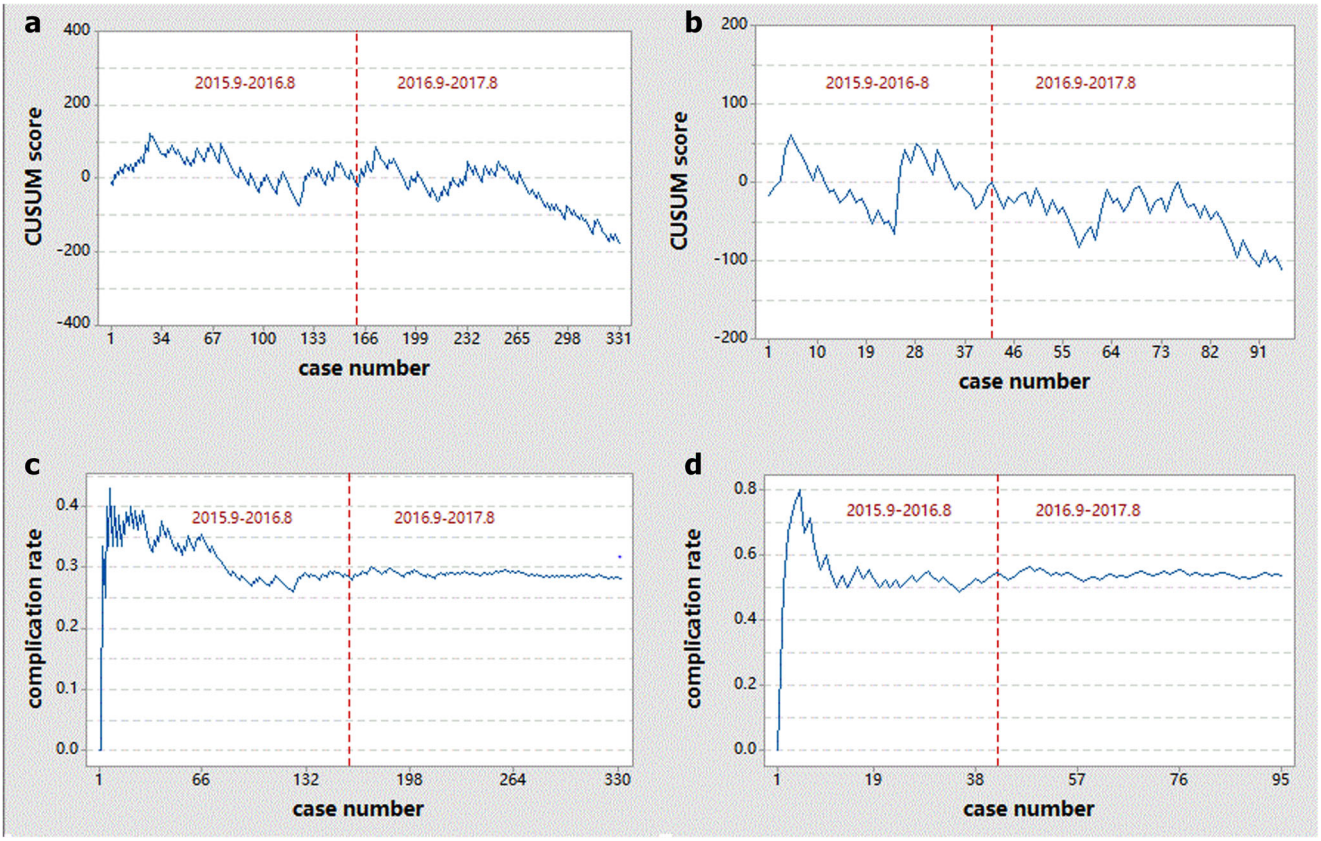

Fig. 3 Monitoring surgical complications. **a** CUSUM score for surgeon A was derived from target value of average CCI (8.5) in the first year (2015.9–2016.8). The final CUSUM score was − 176.2, indicating a decreased CCI compared to the previous year. **b** CUCUM score for surgeon B was derived from a target value of average CCI (16.9) in the first year. The final CUSUM score was − 111.0, indicating a decreased CCI compared to the previous year. **c** Change of complication rate over time for CD surgery with the final rate being 28.1% at case 331. **d** Change of complication rate over time for UC surgery with the final rate being 53.7% at case 95

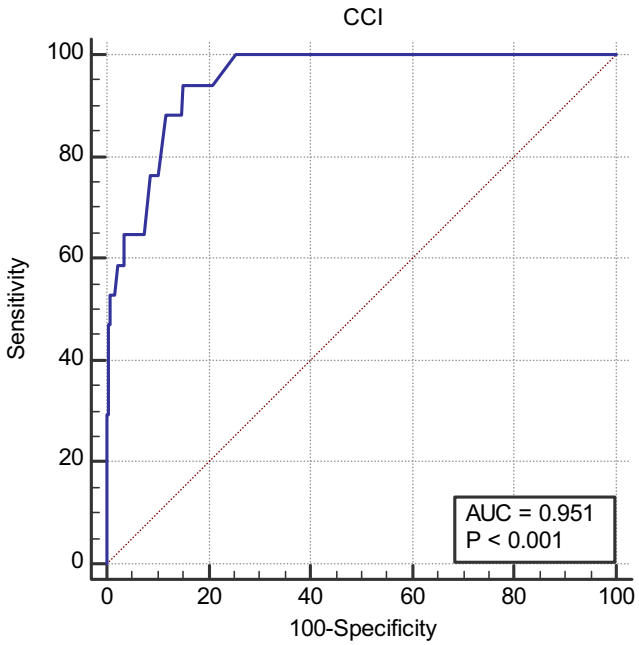

Fig. 4 Receiver operating characteristic curve analysis demonstrated that the CCI value is predictive of prolonged postoperative length of stay. The optimal cutoff value was 24.2 and the area under curve was 0.951 (95% CI 0.925 to 0.970, $p < 0.001$). The sensitivity was 94.1% and the specificity was 85.0%, respectively

represents the proportion of variation explained,[30] the CCI model had a greater goodness of fit compared to the CDC model. This, from another different perspective, reflected the advantage of the CCI system over the conventional CDC grading system.

In terms of monitoring surgical outcomes for individual surgeon, the CCI can be implemented in the CUSUM model. Considering the capability of CCI to reflect the overall magnitude and number of complications, continuous monitoring of the CCI provides more detailed information about surgical performance than monitoring the complication rate alone. Thus, any deviation or lapses in surgical performance will be detected and corrected promptly.

Several limitations must be considered when interpreting the results of our work. First, this is a retrospective design carried out in a single center. Second, continuous monitoring the CCI for a single patient can provide information about changes in the postoperative course over time. This study did not include follow-up of the patients and evaluation of the long-term CCI, leaving the potential advantage of monitoring the CCI unexplored. Third, the CCI has certain drawbacks. For example, reoperation for complications has higher CCI value than non-operative treatment but the decision of surgical intervention is largely affected by the practice of individual surgeon. Therefore, consensus of treatment must be reached regarding different complications. Finally, in some cases, length of stay might be prolonged in patients awaiting rehabilitation or home services, leading to potential bias.

In conclusion, the CCI is applicable in IBD patients who undergo surgery and is more sensitive in reflecting both the number and severity of postoperative complications than the conventional CDC grading system. The CCI is more strongly correlated to postoperative LOS than CDC in multi-complicated patients. Surgeons can in advance identify patients with higher CCI value and initiate radical therapies instead of conservative treatment. In addition, continuous monitoring of the CCI provides surgical quality feedback to individual surgeons.

Author Contributions FZ: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis.

DF: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis.

TZ: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; statistical analysis.

LG: study concept and design; critical revision of the manuscript for important intellectual content.

WZ: analysis and interpretation of data; critical revision of the manuscript for important intellectual content; study supervision.

ZG: analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

YL: analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

JG: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; statistical analysis. Critical revision of the manuscript for important intellectual content. Study supervision.

NL: study concept and design; acquisition of data; critical revision of the manuscript for important intellectual content; study supervision.

JL: study concept and design; acquisition of data; critical revision of the manuscript for important intellectual content; study supervision.

All authors have approved the final version of this manuscript.

Compliance with Ethical Standards

The protocol of this study was approved by the Ethics Committee of Jinling Hospital

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Aarons CB. Laparoscopic surgery for Crohn disease: a brief review of the literature. *Clin Colon Rectal Surg* 2013;26: 122–7
2. Sica GS, Biancone L. Surgery for inflammatory bowel disease in the era of laparoscopy. *World J Gastroenterol* 2013;19: 2445–8
3. Maggiori L, Panis Y. Laparoscopy in Crohn's disease. *Best Pract Res Clin Gastroenterol* 2014;28: 183–194
4. Fichera A. Laparoscopic treatment of Crohn's disease. *World J Surg* 2011 35: 1500–1504
5. 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: 205–213

6. Clavien PA, Barkun J, de Oliveira ML, *et al*. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250: 187–196.
7. Bruce J, Krukowski ZH, Al-Khairy G, *et al*. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br J Surg* 2001;88: 1157–68.
8. Yoon PD, Chalasani V, Woo HH. Use of Clavien-Dindo classification in reporting and grading complications after urological surgical procedures: analysis of 2010-2012. *J Urol* 2013;190: 1271–4.
9. Wechter ME, Mohd J, Magrina JF, *et al*. Complications in robotic-assisted gynecologic surgery according to case type: a 6-year retrospective cohort study using Clavien–Dindo classification. *J Minim Invasive Gynecol* 2014;21: 844–50.
10. Martin RC II, Brennan MF, Jaques DP. Quality of complication reporting in the surgical literature. *Ann Surg* 2002;235: 803–813
11. Slankamenac K, Graf R, Barkun J, *et al*. The Comprehensive Complication Index: a novel continuous scale to measure surgical morbidity. *Ann Surg* 2013;258: 1–7.
12. Slankamenac K, Nederlof N, Pessaux P, *et al*. The comprehensive complication index: a novel and more sensitive endpoint for assessing outcome and reducing sample size in randomized controlled trials. *Ann Surg* 2014;260: 757–762.
13. Kim TH,Suh YS,Huh YJ, *et al*. The comprehensive complication index (CCI) is a more sensitive complication index than the conventional Clavien-Dindo classification in radical gastric cancer surgery. *Gastric Cancer* 2017 21;1–11
14. Fumery M, Seksik P, Auzolle C, *et al*. Postoperative Complications after Ileocecal Resection in Crohn' s Disease: A Prospective Study From the REMIND Group. *Am J Gastroenterol* 2017;112: 337–345
15. Peyrin-Biroulet L, Germain A, Patel AS, *et al*. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. Aliment Pharmacol Ther 2016; 44(8):807–16
16. Penninck E, Fumery M, Armengol-Debeir L, *et al*. Postoperative Complications in Pediatric Inflammatory Bowel Disease: A Population-based Study. *Inflamm Bowel Dis* 2016 22:127–33
17. Couwenberg AM,de Beer FSA,Intven MPW, *et al*. The impact of postoperative complications on health-related quality of life in older patients with rectal cancer; a prospective cohort study. *J Geriatr Oncol* 2017. https://doi.org/10.1016/j.jgo.2017.09.005.
18. Hueting WE, Buskens E, van der Tweel I, *et al*. Results and complications after ileal pouch anal anastomosis: a meta-analysis of 43 observational studies comprising 9,317 patients. *Dig Surg* 2005;22: 69–79
19. Yamamoto T, Spinelli A, Suzuki Y, *et al*. Risk factors for complications after ileocolonic resection for Crohn's disease with a major focus on the impact of preoperative immunosuppressive and biologic therapy: A retrospective international multicenter study. *United European Gastroenterol J* 2016;4: 784–793
20. Ferrante M, de Buck van Overstraeten A, Schils N, *et al*. Perioperative Use of Vedolizumab is not Associated with Postoperative Infectious Complications in Patients with Ulcerative Colitis Undergoing Colectomy. *J Crohns Colitis* 2017;10: 1–9
21. de Buck van Overstraeten A, Mark-Christensen A, Wasmann KA, *et al*. Transanal Versus Transabdominal Minimally Invasive (Completion) Proctectomy With Ileal Pouch-anal Anastomosis in Ulcerative Colitis: A Comparative Study. *Ann Surg* 2017;266: 878–883
22. Gong J, Wei Y, Gu L, *et al*. Outcome of Surgery for Coloduodenal Fistula in Crohn's Disease. *J Gastrointest Surg* 2016;20: 976–84
23. Satsangi J, Silverberg MS, Vermeire S, *et al*. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006;55: 749–753.
24. Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40: 373–83
25. Clavien P, Vetter ÃD, Staiger ÃRD, *et al*. The Comprehensive Complication Index (CCI®): Added Value and Clinical Perspectives 3 Years "Down the Line". *Ann Surg* 2017;265: 1045–1050
26. Yap CH, Colson ME, Watters DA. Cumulative sum techniques for surgeons: a brief review. *ANZ J Surg* 2007;77: 583–6
27. Farmer RG, Hawk WA, Turnbull RB Jr. Indications for surgery in Crohn's disease: Analysis of 500 cases. *Gastroenterology* 1976; 71: 245–250.
28. Kalisvaart M, de Haan JE, Polak WG, *et al*. Comparison of Postoperative Outcomes Between Donation After Circulatory Death and Donation After Brain Death Liver Transplantation Using the Comprehensive Complication Index. *Ann Surg* 2017;266: 772–778
29. Pessaux P, Sauvanet A, Mariette C, *et al*. External pancreatic duct stent decreases pancreatic fistula rate after pancreaticoduodenectomy: prospective multicenter randomized trial. *Ann Surg* 2011;253: 879–85
30. Mittlbock M, Heinzl H. A note on R2 measures for Poisson and logistic regression models when both models are applicable. *J Clin Epidemiol* 2001;54: 99–103