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The influence of early operative treatment on postoperative recurrence in patients with Crohn's disease of the ileocecal region

Утицај раног оперативног лечења на постоперативни рецидив код болесника са Кроновом болешћу илеоцекалне регије

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The influence of early operative treatment on postoperative recurrence in patients with Crohn's disease of the ileocecal region

Утицај раног оперативног лечења на постоперативни рецидив код болесника са Кроновом болешћу илеоцекалне регије

SUMMARY

Introduction/Objective Crohn's disease was traditionally managed by gastroenterologists, but in the past decade the surgeon's role has expanded, with specialized inflammatory bowel disease surgeons now integral to multidisciplinary decision-making. Evidence indicates that early ileocecal resection for localized terminal ileitis with a predominantly fibrotic component, performed before complications arise, may improve outcomes and reduce disease-related morbidity. The aim of this study is to evaluate the impact of early ileocecal resection with Kono-S anastomosis on postoperative disease control in patients with localized Crohn's disease, by assessing changes in inflammatory biomarkers, clinical symptoms, and endoscopic recurrence over a two-year follow-up period.

Methods From 2021 to 2023, all patients in this study were assessed by the Inflammatory Bowel Disease Multidisciplinary Team of the University Clinical Center of Vojvodina, which determined indications for surgery. Postoperative recurrence was monitored clinically and endoscopically using colonoscopy and the Rutgeerts score. Sixty patients underwent laparoscopic ileocecal resection with Kono-S anastomosis.

Results Statistical analyses (IBM SPSS 26) used repeated-measures ANOVA at three time points: preoperatively, one year postoperatively, and two years postoperatively. Fecal calprotectin showed a strong time effect ($F(1.77, 104.51) = 300.13, p < .001, \eta^2 = .84$), demonstrating substantial reduction in intestinal inflammation. Defecation difficulty scores also decreased significantly ($F(1.43, 84.28) = 136.36, p < .001, \eta^2 = .70$). Rutgeerts scores showed no significant change between years one and two ($F(1, 56) = 3.11, p > .05$), indicating stable endoscopic findings.

Conclusion Endoscopic monitoring with the Rutgeerts score, supported by fecal calprotectin, proved most reliable for postoperative surveillance. With careful multidisciplinary selection—especially in patients with localized, fibrotic disease—early ileocecal resection using the Kono-S technique can effectively control Crohn's disease, decrease rehospitalizations and reoperations, and improve quality of life.

Keywords: Crohn's disease; surgical treatment; ileocecal resection; Kono-S anastomosis; Rutgeerts score

САЖЕТАК

Увод/Циљ Кронова болест се традиционално лечила код гастроентеролога, али се током последње деценије улога хирурга значајно проширила, па су специјализовани хирурзи за запаљенске болести црева постали кључни део мултидисциплинарног тима. Докази указују да рана илеоцекална ресекција код локализованог терминалног илеитиса са претежно фиброзном компонентом, изведена пре појаве компликација, може побољшати исходе и смањити морбидитет повезан са болешћу. Циљ ове студије је да се процени утицај ране илеоцекалне ресекције са *Kono-S* анастомозом на постоперативну контролу болести код болесника са локализованом Кроновом болешћу, проценом промена инфламаторних биомаркера, клиничких симптома и ендоскопског рецидива током двогодишњег периода праћења.

Методе У периоду од 2021. до 2023. сви болесници у овој студији процењени су од стране мултидисциплинарног тима за запаљенске болести црева Универзитетског клиничког центра Војводине, који је одређивао индикације за операцију. Постоперативни рецидив праћен је клинички и ендоскопски, помоћу колоноскопије и Рутгертсовог скорa. Шездесет болесника је подвргнуто лапароскопској илеоцекалној ресекцији са *Kono-S* анастомозом.

Резултати Коришћен је *ANOVA* тест поновљених мерења у три временске тачке: преоперативно, годину дана постоперативно и две године постоперативно. Фекални калпротектин је показао снажан ефекат времена ($F(1.77, 104.51) = 300.13, p < .001, \eta^2 = 0.84$), указујући на значајно смањење интестиналне инфламације. Скорови отежаног пражњења такође су се значајно смањили ($F(1.43, 84.28) = 136.36, p < .001, \eta^2 = 0.7$). Рутгертсови скорови нису показали значајну промену између прве и друге године ($F(1, 56) = 3.11, p > 0.05$), што указује на стабилне ендоскопске налазе.

Закључак Ендоскопско праћење помоћу Рутгертсовог скорa, уз подршку фекалног калпротектина, показало се најпоузданијим за постоперативни надзор. Уз пажљив мултидисциплинарни одабир, посебно код болесника са локализованом, фиброзном болешћу, рана илеоцекална ресекција техником *Kono-S* може ефикасно контролисати Кронову болест, смањити рехоспитализације и реоперације и побољшати квалитет живота.

Кључне речи: Кронова болест; хируршко лечење; илеоцекална ресекција; *Kono-S* анастомоза; Рутгертсов скор

INTRODUCTION

The incidence and prevalence of Crohn's disease have been rising globally, with annual increases in incidence reported between 4% and 15% over the past three decades. Crohn's disease represents a substantial socioeconomic and healthcare burden worldwide, primarily because it affects a young, working-age population and follows a chronic, relapsing–remitting course characterized by periods of exacerbation and remission [1, 2]. Despite significant advances in medical therapy, approximately 25% of patients require surgical intervention within ten years of diagnosis, and nearly 20% of those who undergo surgery require reoperation within five years [3, 4].

Historically, Crohn's disease was managed predominantly by gastroenterologists, who were responsible for diagnosis, pharmacological treatment, and follow-up, while surgeons were mainly involved in addressing acute complications. These often resulted in multiple resections, high-output ileostomies, and, in some cases, short bowel syndrome. Over the past decade, however, the surgeon's role has evolved substantially. The emergence of the inflammatory bowel disease (IBD) surgeon specialized in the surgical management of these patients has transformed Crohn's disease's care into a multidisciplinary effort involving gastroenterologists, surgeons, radiologists, pathologists and anesthesiologists [5, 6].

A major challenge in Crohn's disease management remains its nonspecific clinical presentation and delayed diagnosis. On average, two years elapse between the onset of initial symptoms (such as diarrhea, hematochezia, or nonspecific abdominal pain) and the establishment of a definitive diagnosis. This delay often results in missed therapeutic opportunities and the development of complications including stenosis, fistulas, abscesses, and perforations [7].

Histopathological examinations have demonstrated that intestinal lesions in Crohn's disease may be predominantly inflammatory, mixed, or fibrotic. While inflammatory changes may respond favorably to anti-inflammatory or biological therapy, the mixed and fibrotic types typically show poor or no response to medical treatment, necessitating interventional management such as endoscopic dilation or surgery [8]. The largest study on balloon dilation in Crohn's disease, conducted by Bettenworth et al. (2017), included 1,493 patients who underwent 3,213 endoscopic balloon dilations. Although the initial success rate was high, 73.5% required redilation within 24 months, and 42.9% ultimately required surgical resection [9].

Consequently, recent studies have reconsidered early ileocecal resection for localized terminal ileitis with predominant fibrotic involvement, before the onset of complications or complete obstruction. This strategy may improve quality of life and prevent disease progression to

fistulizing or perforating forms that require urgent, extensive resections, high-output ileostomies, or result in short bowel syndrome [10,11]. Increasing attention has also been directed to the potential influence of anastomotic technique and mesenteric involvement on disease recurrence. To date, no specific anastomotic configuration has been conclusively shown to reduce the rate of postoperative recurrence [12].

The Kono-S anastomosis, first described in 2011, has since demonstrated favorable outcomes worldwide. This technique forms a “supporting column” of bowel that maintains luminal diameter and prevents restenosis. The mesenteric side is positioned centrally within this column, such that even in cases of mesenteric recurrence, the anastomotic lumen remains patent, thereby reducing the risk of restenosis, a limitation observed in conventional end-to-end or side-to-side anastomoses [13].

The aim of this study is to evaluate the impact of early ileocecal resection with Kono-S anastomosis on postoperative disease control in patients with localized Crohn’s disease, by assessing changes in inflammatory biomarkers, clinical symptoms, and endoscopic recurrence over a two-year follow-up period.

METHODS

Between 2021 and 2023, all patients included in this study were reviewed at the Inflammatory Bowel Disease Multidisciplinary Team (IBD-MDT) Conference of the University Clinical Center of Vojvodina, where operative management was discussed and approved.

Prior to surgery, all patients underwent colonoscopy, which confirmed stenosis with a predominant fibrotic component; in most cases, the lumen was impassable to the colonoscope. None of the patients had undergone preoperative endoscopic balloon dilation. As part of the preoperative assessment, all patients also underwent magnetic resonance enterography to determine the location and length of the affected intestinal segment.

Exclusion criteria included multiple disease localizations and previous bowel resections for Crohn's disease. The presence of fistulas or abscesses was considered a conditional exclusion criterion; in such cases, the decision regarding surgical treatment was made on a case-by-case basis after multidisciplinary discussion. For patients receiving corticosteroid therapy, tapering was performed preoperatively to minimize the risk of postoperative complications while avoiding inflammatory exacerbation. Ongoing anti-TNF therapy was not considered a contraindication for primary anastomosis formation [11].

Postoperative recurrence was evaluated by the following:

- Endoscopy, using colonoscopic findings and the Rutgeerts scoring system;
- Laboratory parameters, including complete blood count (CBC), C-reactive protein (CRP), and fecal calprotectin;
- Clinical assessment, based on patient-reported bowel function scored subjectively on a 1–10 scale.

All patients underwent laparoscopic ileocecal resection with construction of a Kono-S anastomosis (Figure 1). An Enhanced Recovery After Surgery (ERAS) protocol was applied in all cases, with oral intake initiated on the evening of surgery. Upon discharge, patients received metronidazole 400 mg twice daily for 14 days.

Postoperative initiation of biological therapy was determined according to the American Gastroenterological Association risk stratification for postoperative recurrence [14].

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). To evaluate changes over time, repeated-measures analyses of variance (ANOVA) were conducted for each inflammatory and clinical parameter, including leukocyte count, C-reactive protein (CRP), fecal calprotectin, and defecation difficulty scores. The Rutgeerts score, which was assessed postoperatively to evaluate endoscopic recurrence at the anastomotic site, was analyzed across the two available follow-up time points (T2 and T3).

Mauchly's test of sphericity was used to assess the assumption of sphericity for each repeated-measures ANOVA. When this assumption was violated ($p \leq 0.05$), the Greenhouse–Geisser correction was applied to adjust the degrees of freedom. When the assumption was met ($p > 0.05$), results from the sphericity-assumed model were reported.

If a significant main effect of time was identified, Bonferroni-adjusted pairwise comparisons were conducted to determine the specific time points between which differences occurred. Effect sizes were expressed as partial eta squared (η_p^2) and interpreted according to Cohen's (1988) conventions: 0.01 = small, 0.06 = medium, and 0.14 = large effect.

Ethics: This study was conducted in accordance with the principles of the Declaration of Helsinki. The research protocol was reviewed and approved by the Ethics Committee of the University Clinical Center of Vojvodina (protocol number: 00-418).

RESULTS

A total of 60 patients were included in the study. Baseline demographic, disease, and treatment characteristics are summarized in Table 1. All patients underwent laparoscopic ileocecal resection with Kono-S anastomosis.

A repeated-measures analysis of variance (ANOVA) was performed to examine changes in inflammatory and clinical parameters across three assessment points: before surgery (T1), one year after surgery (T2), and two years after surgery (T3).

The repeated-measures ANOVA revealed a significant main effect of time for leukocytosis ($F(1, 59) = 14.75, p < 0.001, \eta_p^2 = 0.20$), indicating a postoperative reduction in leukocyte count. Bonferroni-adjusted post hoc comparisons showed a significant decrease from the preoperative assessment to one year postoperatively ($p < 0.001$), with no further significant change between one and two years after surgery ($p > 0.05$).

CRP levels also changed significantly over time ($F(1.56, 92.45) = 34.98, p < 0.001, \eta_p^2 = 0.37$), demonstrating a sustained reduction at both postoperative time points. A particularly strong time effect was observed for fecal calprotectin ($F(1.77, 104.51) = 300.13, p < 0.001, \eta_p^2 = 0.84$), indicating a marked and continuous decline in intestinal inflammation across all assessments. Defecation difficulties similarly improved over time ($F(1.43, 84.28) = 136.36, p < 0.001, \eta_p^2 = 0.70$), reflecting enhanced bowel function one and two years postoperatively (Table 2).

In contrast, the Rutgeerts score, assessed only postoperatively to evaluate endoscopic recurrence at the anastomotic site, showed no significant difference between the one-year and two-year follow-ups ($F(1, 56) = 3.11, p > 0.05, \eta_p^2 = 0.05$), suggesting stable endoscopic findings during the observation period.

Overall, effect sizes ranged from moderate (leukocytosis) to very large (fecal calprotectin and defecation difficulties), indicating substantial variation in the magnitude of postoperative improvement across parameters.

DISCUSSION

Recent studies have suggested that early ileocecal resection may lead to better disease control, a lower rate of repeat surgery, and reduced overall treatment costs compared with resections performed at more advanced stages of Crohn's disease. These findings are supported by data from Sweden and other population-based cohorts, which indicate improved surgical outcomes and a declining need for re-resections in recent decades [15, 16]. Our results are consistent with these observations. In our study, all patients underwent surgery at an early disease stage before

the development of complications such as abscesses, fistulas, or bowel obstruction that could otherwise necessitate multiple operations. During the follow-up period, no patient required re-operation, reflecting the potential benefit of early surgical intervention.

In all cases, a Kono-S anastomosis was performed. Because postoperative recurrence frequently develops at the anastomotic site, its configuration remains an important determinant of long-term outcome. Kono-S technique creates a mesenteric “supporting column” designed to maintain luminal patency and potentially reduce subocclusive symptoms. In our series, patient-reported bowel function improved compared with preoperative status. However, comparative effectiveness data remain inconclusive. The large, propensity-matched KoCoRICCO study found no significant reduction in postoperative endoscopic recurrence with Kono-S compared with conventional anastomoses [17]. Conversely, other observational studies and systematic reviews, such as that of Lingam et al., have reported potential functional and patency-related advantages, although the evidence quality remains low and randomized data are lacking [18]. Our results therefore support the feasibility and functional safety of Kono-S but cannot confirm superiority in preventing recurrence.

For postoperative recurrence monitoring, inflammatory markers (CRP, leukocyte count, and fecal calprotectin) were assessed alongside scheduled endoscopic evaluations at 12 and 24 months. While systemic inflammatory markers are not sufficiently specific for detecting endoscopic recurrence, they remain useful for identifying complications such as abscesses or fistulas. In contrast, endoscopic evaluation using the Rutgeerts score, combined with fecal calprotectin values, provided a reliable measure of mucosal recurrence. A Rutgeerts score > 2 at the anastomosis clearly indicated endoscopic recurrence. When compared with the results reported by Bak et al., who observed higher rates of endoscopic inflammation and re-resection during long-term follow-up [19], our recurrence rate was lower.

However, several factors must be acknowledged: our follow-up period was shorter (2 years versus 5 years in their study), and our cohort was more selectively defined, excluding patients with prior resections or multiple disease localizations. These methodological differences likely contributed to the favorable outcomes observed in our patient population.

CONCLUSION

Early ileocecal resection with Kono-S anastomosis in patients with localized, predominantly fibrotic Crohn’s disease provides effective postoperative disease control, demonstrated by significant improvement in inflammatory markers and stable endoscopic findings during two-year

follow-up. In the authors' experience, structured postoperative surveillance based on the Rutgeerts score and fecal calprotectin represents a reliable and practical monitoring protocol.

Conflict of interest: None declared.

Paper accepted

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Table 1. Baseline demographic and disease characteristics

Variable	Value
Number of patients	60
Sex, n (%)	Male: 15 (25%) Female: 45 (75%)
Disease location	Localized ileocecal Crohn's disease (100%)
Disease phenotype	Predominantly fibrotic stenosis
Preoperative colonoscopic finding	Stenosis in all patients
Preoperative endoscopic balloon dilation	None
Previous bowel resection for Crohn's disease	None
Multiple disease localizations	Excluded

Table 2. Changes in inflammatory and clinical indicators before and after surgery: Results of repeated measures ANOVA

Variable	Time	M (SD)	Mauchly W	F	df1, df2	p	η_p^2	T1	T2	T3
Leukocytosis	T1	0.3 (0.46)	0.00*	14.75	1, 59	< 0.001	0.2	–	< 0.001	< 0.001
	T2	0.1 (0.3)						–	–	
	T3	0.1 (0.3)						–		–
C-reactive protein	T1	0.6 (0.74)	0.72**	34.98	1.56, 92.45	< 0.001	0.37	–	< 0.001	< 0.001
	T2	0.25 (0.44)						–	< 0.05	
	T3	0.15 (0.36)						–		–
Fecal calprotectin	T1	2.2 (0.94)	8.01*	300.13	1.77, 104.51	< 0.001	0.84	–	< 0.001	< 0.001
	T2	0.85 (0.66)						–	< 0.001	
	T3	0.4 (0.49)						–		–
Defecation difficulties score	T1	1.2 (0.76)	29.63**	136.36	1.43, 84.28	< 0.001	0.7	–	< 0.001	< 0.001
	T2	0.35 (0.48)						–	< 0.01	
	T3	0.2 (0.40)						–		–
Rutgeerts score	T1	–	1.00	3.11	1, 56	0.08	0.05	–	–	–
	T2	1.16 (0.68)						–	> 0.05	
	T3	1.11 (0.65)						–		–

T1 – before surgery; T2 – 1 year after surgery; T3 – 2 years after surgery; W – Mauchly's test of sphericity; η_p^2 – partial eta squared; M – mean; SD – standard deviation;

*p < 0.05;

**p < 0.01

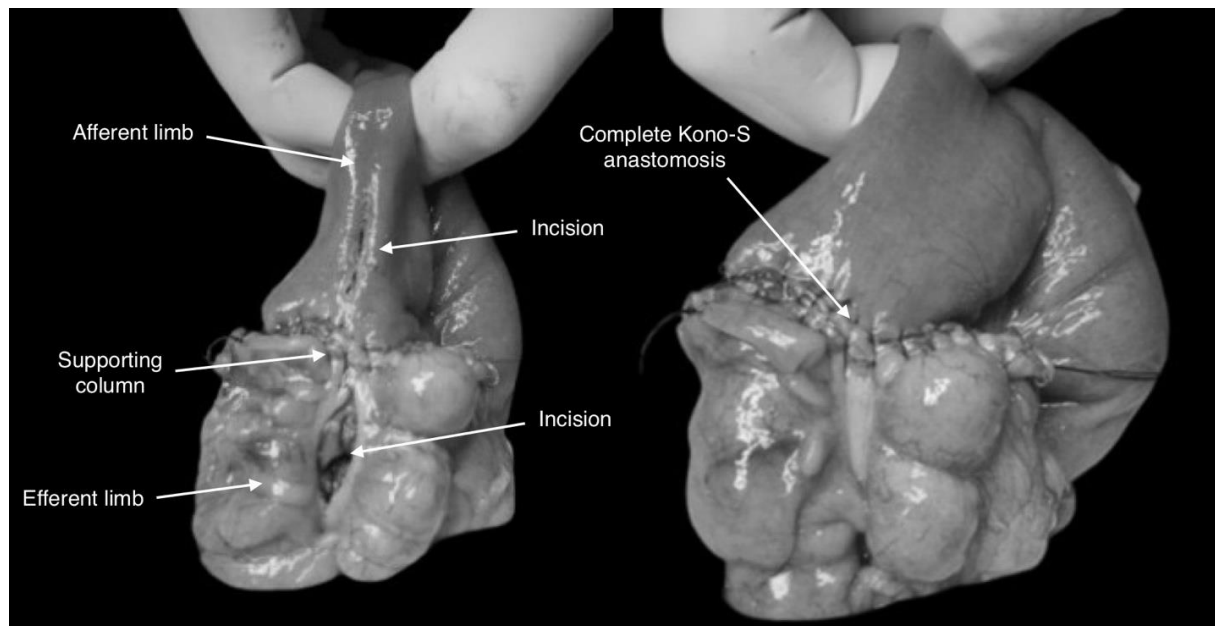


Figure 1. Kono-S anastomosis