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Intraoperative endoscopy is safe and helps to determine the resection extent in Crohn's disease

Intraoperačná enteroskopia je bezpečná a je prínosom v určení rozsahu resekčného výkonu pri Crohnovej chorobe

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Summary: **Background:** Intraoperative endoscopy can be of value in determining the extent of resection in Crohn's disease (CD) patients, but data on its safety and usefulness in this setting are scarce. The aims of this study were first to analyse the safety of intraoperative endoscopy and then determine its impact on the extent of the resection. **Patients and Methods:** CD patients operated on in one centre between January 2015 and December 2016 were included. The differences in postoperative course and complications between the endoscopy group and the non-endoscopy group were analysed. In addition, the impact of intraoperative endoscopy findings on the extent of the resection was determined. **Results:** In total, 46 CD patients underwent surgery and 25 intraoperative endoscopies were performed in 20 patients. The endoscopy group had a significantly longer median hospital stay than the non-endoscopy group (respective medians of 6.5 vs. 5 days; p = 0.019). There were no significant differences between the two groups in other parameters. In 12 of the 20 patients in the endoscopy group, information provided by endoscopy led to change in the extent of resection. **Conclusion:** Intraoperative endoscopy is a safe and useful tool for tailoring the extent of surgery in CD patients.

Key words: intraoperative endoscopy – Crohn's disease – surgery

Súhrn: **Úvod:** Intraoperačná enteroskopia môže byť nápomocná pri určení rozsahu resekcie u pacientov s Crohnovou chorobou, ale údaje o jej bezpečnosti a prínose nie sú dostatočné. Cieľom našej štúdie bolo, po prvé, analyzovať bezpečnosť intraoperačnej endoskopie, po druhé zistiť vplyv na určenie rozsahu resekcie. **Pacienti a metódy:** Do štúdie boli zahrnutí všetci pacienti operovaní v jednom referenčnom centre od januára 2015 do decembra 2016. Rozdiely medzi intraoperačne endoskopovanou a neendoskopovanou skupinou v pooperačnom priebehu boli vyhodnotené štatisticky a vyhodnotený bol aj vplyv intraoperačnej endoskopie na rozsah resekčného výkonu. **Výsledky:** Spolu 46 pacientov s Crohnovou chorobou podstúpilo operáciu. Vykonaných bolo 25 intraoperačných endoskopií u 20 pacientov. Medián dĺžky hospitalizácie v endoskopovanej skupine pacientov bol signifikantne dlhší ako v neendoskopovanej skupine (6,5 vs. 5 dní; p = 0,019), iné rozdiely v pooperačnom priebehu neboli detekované. Intraoperačná endoskopia viedla v 12 prípadoch z 20 endoskopovaných pacientov k zmene rozsahu resekcie. **Záver:** Intraoperačná endoskopia je bezpečná a užitočná pomôcka na určenie rozsahu chirurgickej liečby komplikovanej Crohnovej choroby.

Kľúčové slová: intraoperačná enteroskopia – Crohnova choroba – operácia

Introduction

Crohn's disease (CD) represents a chronic inflammatory condition affecting any part of the gastrointestinal tract. Despite great effort invested in the research of the disease pathogenesis over past years, the disease course remains unpredictable and only partially influenced by current therapeutic strategies [1]. Typically, during the disease course the disease behaviour changes towards the

stricturing and penetrating phenotype in nearly half of CD patients after 10 years following diagnosis [2]. This change in disease behaviour leads to complications, mainly intestinal stenosis and intra-abdominal abscess. In the case of fibrotic stenosis with obstructive symptoms, surgical resection or stricturoplasty remains the only therapeutic option thus far [3]. For intra-abdominal abscess complicating penetrating CD phenotype, percutaneous or surgical drainage is the first step followed by the escalation of anti-inflammatory therapy and in some cases a delayed planned resection [4].

The determination of the extent of the surgical resection remains a matter of debate, although it has become clear that no "clear margin" resection approach is beneficial [5] in terms of prevention of long-term post-surgical disease recurrence. Thus, currently in the majority of cases the preoperative assessment of the localisation and extent of the stenosis is done by means of cross-sectional imaging, preferentially magnetic resonance imaging (MRI), together with preoperative endoscopic assessment.

Both, MR enterography as well as ileo-colonoscopy represent a cumbersome procedure for the patient as both procedures require preparation with laxatives which can be difficult to complete for a patient with stricturing bowel disease. In addition, the procedures themselves are often limited in quality and incomplete in this specific patients' population, although no specific data regarding this clinical setting are available. For the specific evaluation of the extent of small bowel disease, enteroscopy, especially double balloon enteroscopy, has been shown to be equally safe and effective in various conditions as compared to intraoperative enteroscopy [6,7] but the number of CD evaluated specifically with the intention of preoperative assessment was limited in this study. Finally, depending on the local health care structure and organisation, many CD patients with stricturing disease may consult the referral centre with surgical expertise in a clinical situation that requires immediate intervention. Therefore, preoperative assessment of the disease extent might sometimes not be possible or of low quality due to the mentioned reasons.

Furthermore, the sensitivity and specificity of preoperative assessment of disease extent by means of MR enterography varies across the studies [8] and is generally rather low when compared with the intraoperative judgement [9,10]. Especially in extensive disease, MR enterography seems to overestimate the length of the involved segment, however, underestimation may also occur in approximately one tenth of cases [9].

Thus, the thorough intraoperative assessment of the disease extent still represents an important part in the process of tailoring the type and extent of surgery in complicated CD. Intraoperative endoscopic assessment has been shown to be of additional value for intraoperative decision-making [11,12] but its safety has been questioned [13] mainly based on data on morbidity and mortality of intraoperative enteroscopies performed in obscure gastrointestinal bleeding conditions. Taking all factors into account, data on the safety of intraoperative endoscopic assessment of disease extent in the particular setting of CD are lacking and this procedure might be of additional value for the intraoperative decision-making on the extent of surgical resection.

Therefore, the aim of our study was firstly to determine the safety of intraoperative endoscopic assessment of disease activity and extent in CD patients undergoing surgery due to the stricturing or penetrating disease complication. Secondly, we evaluated its impact on the extent of the resection.

Patients and Methods

In a retrospective cohort study, all CD patients operated on in one centre between January 2015 and December 2016 were identified through diagnosis coding used for insurance purposes. CD patients indicated for surgical intervention due to stricturing or penetrating disease complications or failure of medical therapy were eligible for further analysis.

The decision on the type and extent of the surgery was based on the multidisciplinary discussion of dedicated surgeons, gastroenterologists and radiologists. Intraoperative endoscopy was performed in case of unclear disease extent based on the preoperative MRI, when a recent MRI and/or endoscopy was not available or in case of previously detected extended small bowel disease (i.e. disease involving more than 30 cm of terminal ileum). The extent of the resection in each procedure was first evaluated by the surgeon, subsequently the extent was determined by the intraoperative endoscopy and the differences between the two evaluations were noted in the endoscopy report.

For the primary aim of the study, the duration of operation, hospital stay and complications such as anastomotic leak, abscess, readmission within 30 days were noted together with C reactive protein, procalcitonine and white blood cells during the days following the surgical intervention. With regards to the secondary aim of the study, for each endoscopic procedure, the impact on the intraoperative decision-making was noted.

The differences between the group of CD patients who underwent intraoperative endoscopy (endoscopy group) vs. the group without endoscopic assessment were analysed statistically.

Results

In total, 46 CD patients were included (basic demographics are shown in Tab. 1). There were 29 laparotomies

(63%), 10 laparoscopic (21.7%) and 7 single port laparoscopic surgeries (15.3%) due to stricturing (26 patients) and penetrating (18 patients) disease complications or medical treatment failure (2 patients). Twenty-five intraoperative endoscopies were performed in 20 patients (14 enteroscopies, 3 gastroscopies – all three combined with enteroscopies, 11 colonoscopies). Out of 11 enteroscopies, there were 3 push enteroscopies using the oral route and 8 enteroscopies were performed using surgical enterotomy; in 3 cases the full length of the small bowel was examined (Fig. 1). Patients in endoscopy did not differ from the patients in non-endoscopy group with regards to basic demographics, more specifically, age, gender, surgical approach (laparoscopic vs. laparotomy), the number of previous surgical interventions and disease behaviour, i.e. stricturing vs. penetrating disease. A significantly lower proportion of patients with ileocecal disease localisation underwent intraoperative endoscopy (29% of all ileocecal localisation patients underwent endoscopy vs. 67% of all other localisations; p = 0.012), other disease phenotypes did not differ between the two groups.

The endoscopy group had significantly longer median hospital stay compared with the group without endoscopy (respective medians of 6.5 vs. 5 days; p = 0.019; Graph 1A). There were no significant differences between the two groups with regards to the duration of the surgery (respective medians 160 vs. 135 min – endoscopy vs. no endoscopy group; p = n.s.; Graph 1B). C reactive protein, procalcitonine levels and white blood cells were numerically higher in the endoscopy group during the first 5 postoperative days but the difference was not statistically significant.

The subgroup of 11 patients who underwent intraoperative enteroscopy was analysed separately. The entero-

Tab. 1. Basic demographics of the study population.
Tab. 1. Základné demografické údaje o študovanej populácii.

n	**46**
median age (years; min.–max.)	32 (21–70)
males/females (% of males)	17/29 (37%)
disease localization	
• upper gastrointestinal tract	5
• terminal ileum	2
• ileocolonic disease	38
• colonic disease	6
• perianal disease	10
previous surgery	21 (46%)
• 1 resection	12 (26%)
• 2 resections	5 (11%)
• ≥ 3 resections	4 (8%)
reason for surgery	
• stricturing complications	26
• penetrating complications	18
• failure of medical management	2
type of current surgery*	
• ileo-cecal resection	28 (61%)
• colectomy**	18 (40%)
• multiple small bowel segment resection	12 (26%)

* multiple interventions performed in several patients
** various extent of large bowel resections

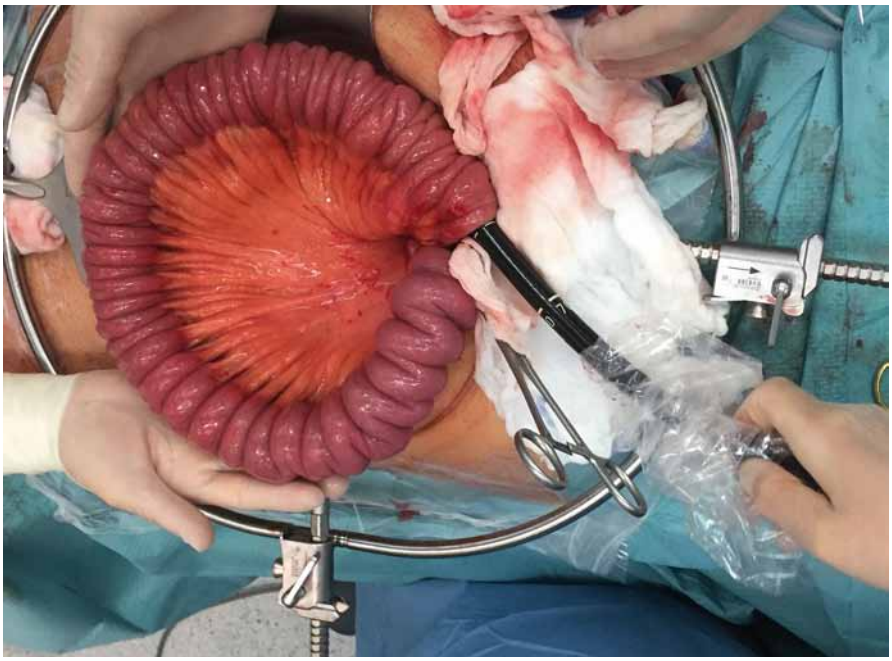
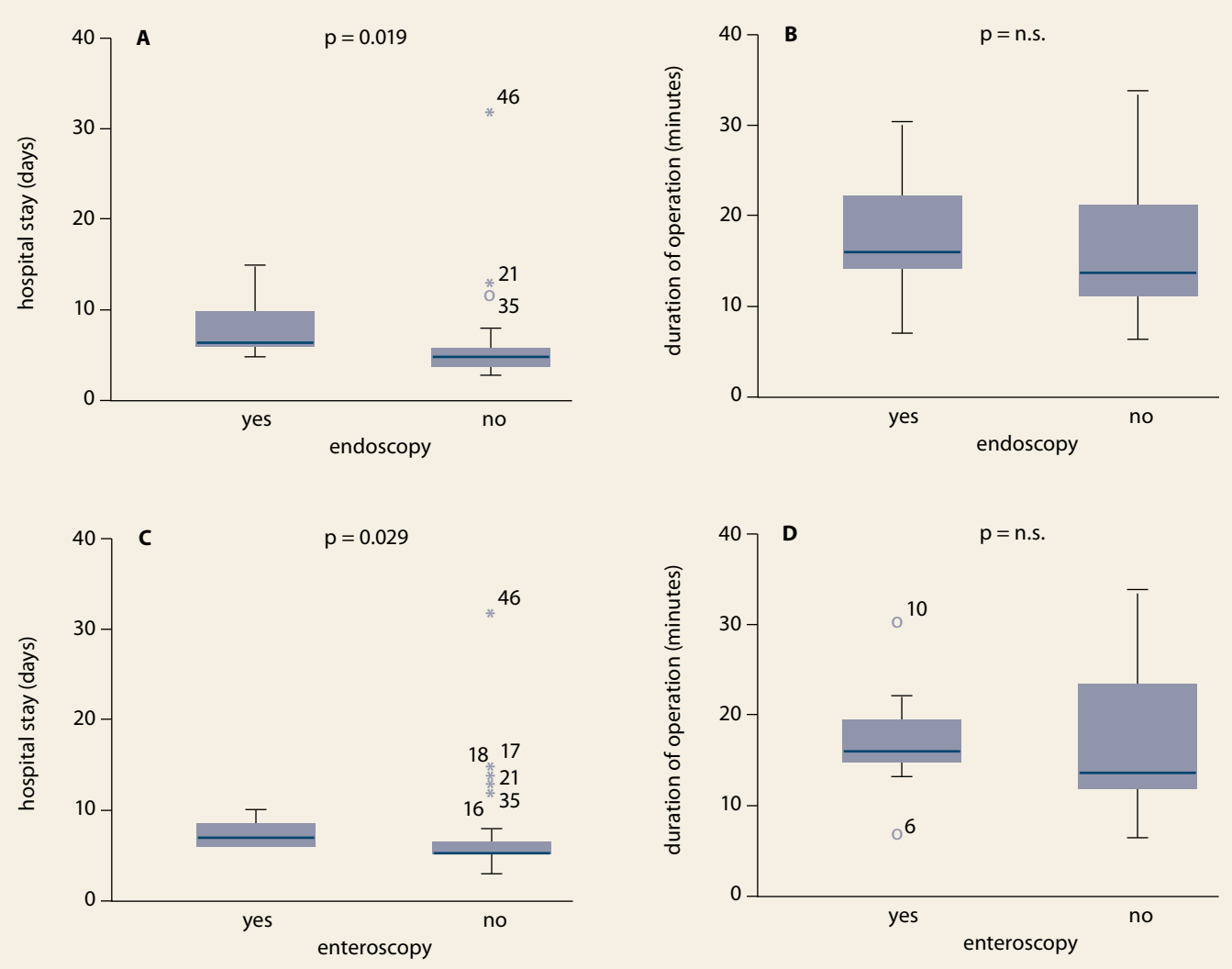


Fig. 1. Position of colonoscope in full enteroscopy to duodenum from ileotomy with external assistance in open laparotomy resection setting.
Obr. 1. Zobrazenie koloskopu pri plnej enteroskopii retrográdne z enterotómie do duodena s externou asistenciou operatéra pri laparotómii.



Graph 1. Comparison of hospital stay and duration of operation between endoscopy and non-endoscopy groups (A and B), and between enteroscopy and non-enteroscopy groups (C and D). Hospital stay was significantly longer for both endoscopy and enteroscopy vs. non-endoscopy and non-enteroscopy group.

Graf 1. Porovnanie dĺžky hospitalizácie a operačného času medzi endoskopovanou a neendoskopovanou skupinou (A a B), a medzi enteroskopovanou a neenteroskopovanou skupinou (C a D). Dĺžka hospitalizácie bola signifikantne dlhšia tak u všeobecne endoskopovaných ako aj špecificky enteroskopovaných pacientov v porovnaní so skupinou bez intraoperačnej endoskopie.

scopy group had significantly longer hospital stay compared with the no enteroscopy group (respective medians 7 vs. 5 days; p = 0.029; Graph 1C). The duration of surgery did not differ between the enteroscopy and no enteroscopy groups (respective medians 160 vs. 135 min; p = n.s.; Graph 1D) and no differences were found between the C reactive protein, procalcitonine levels and white blood cells count between the two groups.

Complications occurred in one out of 20 patients in the endoscopy group (intra-abdominal abscess) and in one out of 26 patients in the non-endoscopy group (bleeding from the anastomosis); p = n.s. There was one readmission in the endoscopy group within 5 days after discharge; the reason was fever diagnosed as based on viral upper respiratory tract infection that was considered unrelated to the surgical procedure.

In 12 out of 20 patients (60%) who underwent intraoperative endoscopic assessment the information provided by endoscopy led to change in the extent of resection (5 reductions and 7 extensions of the segment to be resected) compared with the extent planned based on the cross-sectional imaging and the intraoperative judgement by surgeon.

Discussion

In this retrospective study we show that intraoperative endoscopic assessment of the extent of CD is safe in terms of short term postoperative complications. In addition, the information provided by intraoperative endoscopic assessment is crucial for the intraoperative decision-making on the extent of the surgery in 60% of patients.

Intraoperative endoscopy, more specifically enteroscopy, was historically mainly used for the assessment of the origin of small intestinal bleeding in life threatening obscure gastrointestinal bleeding [13]. In these cohorts, the intraoperative endoscopy was related to a considerable morbidity and mortality of 5% and 17%, resp. [14]. Considering the clinical setting of a patient with gastrointestinal bleeding, this high mortality and morbidity might be inherent to the underlying condition rather than reflecting the risk profile of the procedure itself. Indeed, in our cohort, in line with two other previously published cohorts, this procedure seems to be safe.

In our cohort, the only negative outcome the intraoperative enteroscopy and endoscopy in general were associated with was longer hospital stay. Considering the design of this retrospective cohort, the difference between endoscopy and no endoscopy group in terms of hospital stay might be resulting from selection bias with a priori more complicated cases being selected for intraoperative endoscopic evaluation.

Another important aspect of intraoperative endoscopic assessment that was not dealt with in our study is the information that this assessment provides to treating gastroenterologists for the postoperative medical management. Device-assisted enteroscopies are invasive procedures that can be replaced by intraoperative assessment in patients with an indication for surgery. Such detailed information about the extent of the disease is hardly available with current preoperative assessment and the findings at the intraoperative enteroscopy might shift the therapeutic decision about postoperative management. Considering the reassuring safety data of intraoperative enteroscopy based on this retrospective cohort, we believe a prospective assessment of this particular value of intraoperative enteroscopy is justified. Furthermore, a prospective setting would be able to determine the phenotype of CD patient who would benefit most from the intraoperative endoscopy which we were not able to provide with the present data.

In conclusion, intraoperative endoscopic assessment of the extent of CD does not bring additional complications and helps to better tailor the surgical decision in more than half of patients.

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