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This Newsletter is written by a surgeon. Although, the majority of readers are probably gastroenterologists, I hope you all will find something of interest. That means less about medical treatment and more about surgery and long-term results. I have allowed myself to include articles also from last Autumn.

The last months have been influenced by the pandemic. In times of limited resources, IBD patients are usually down prioritized for surgery, since the cancer patients come first. Young people, deteriorating while standing on the waiting-list, ending up with a stoma that was not planned from the beginning. Luckily, at Karolinska University Hospital, we have had a surprisingly good situation and patients with IBD have been offered surgery when needed.

I have included two articles on COVID-19 in IBDpatients. Further, two articles, in my mind important before surgery, one on surgical technique and the rest on long-term results with or without surgery. ▶

GUT HEALTH
LEGACY, COMMITMENT, INNOVATION

- The selection of articles might be influenced by my interests; laparoscopic surgery in IBD (and cancer) patients, with a special interest in laparoscopic pouch surgery, and preoperative optimization (especially in elderly). The goal is to optimize the patients before the surgical trauma, to reduce the stress and metabolic response in order to limit the risks for complications and improve recovery.

I use the following well known abbreviations:

ART	Assisted Reproductive Technology
CD	Crohn's disease
CI	Confidence Interval
IAAP	Ileal pouch-anal anastomosis
IBD	Inflammatory Bowel Disease
IVF	In Vitro Fertilization
MDT	Multi-Disciplinary Team
OR	Odds Ratio
PSC	Primary Sclerosing Cholangitis
UC	Ulcerative colitis

1) COVID 19

Incidence, outcomes, and impact of COVID-19 on inflammatory bowel disease: propensity matched research network analysis.

HADI Y, ET AL. ALIMENT PHARMACOL THER 2022 JAN;55(2):191-200. DOI: 10.1111/APT.16730.

In this retrospective propensity score matched cohort study utilizing the multi-institutional research network (TriNetX), COVID-19 patients with and without IBD were identified. The TriNetX includes data from more than 40 million patients in the US.

The incidence rate ratio for COVID-19 was lower in IBD patients compared to the non-IBD population (0.79, 95 % CI: 0.72-0.86). COVID-19 patients with IBD were at increased risk for requiring hospitalization compared to non-IBD population (RR: 1.17, 95 % CI: 1.02-1.34) with no differences in need for mechanical ventilation or mortality. IBD patients on steroids were at an increased risk for critical care need (RR: 2.22, 95 % CI: 1.29-3.82). Up to 7 % of patients with IBD and COVID-19 suffered an IBD flare 3-months post-infection. The risk for incident IBD diagnosis after COVID-19 was smaller than in the patients without COVID-19.

REFLECTION

It is reassuring that IBD patients seem to avoid COVID-19 better than average. 2.09 % of the IBD patients vid COVID-19 died and the mortality was not significantly higher than in patients without IBD (1.84 %). The only factor that could be associated with worse outcome was recent use of steroids.

There is a study on timing of surgery after a COVID-19 infection (COVIDSurg Collaborative, et al. Anaesthesia. 2021) which shows that mortality is increased if patients undergo surgery earlier than 7 weeks after COVID-19 infection. A newer study, when most patients are vaccinated, and the virus variant is changed, would probably give different results. However, newer data is, as far as I know, not available.

2) COVID 19

Implementation and short-term adverse events of anti-SARS-CoV-2 vaccines in Inflammatory Bowel Disease patients: an international web-based survey.

ELLUL P, ET AL. CROHNS COLITIS. 2022 JAN 17:JJAC010. DOI: 10.1093/ECCO-JCC/JJAC010. ONLINE AHEAD OF PRINT.PMID: 35037033

3272 IBD patients anonymously completed the survey about vaccination against COVID-19. 80 % had received at least one dose, and 72 % had received two doses of vaccine.

Patients over 60 years old had a significantly higher rate of vaccination ($p<0.001$). Worries before vaccination were; having worse vaccine-related adverse events due to their IBD (25 %), an IBD flare after vaccination (21 %) and, reduced vaccine efficacy due to immunosuppression (18 %).

After the first dose of the vaccine, 72 % had local symptoms and 51 % had systemic symptoms. Five

patients had thrombosis (the severity was not specified). After the second dose, adverse events were less frequent (46 % for local and 42 % for systemic symptoms). 19 % of patients had to miss work at least once.

Use of biological (as a monotheraphy) was a risk factor for adverse events. Active disease at baseline was a risk factor for need of hospitalization.

Nevertheless, few patients were hospitalized (0.3 %), needed a consultation (4 %) or had to change IBD therapy (13 %) after COVID-19 vaccination.

In comparison to other big studies, the risk for adverse events was not higher for IBD patients (compared to the general population).

REFLECTION

These data (still accepted manuscript) support that the COVID-19 vaccines are safe in IBD patients. Of the patients that answered this web-based questionnaire, 80 % had had at least one vaccination and 72 % had got two shots. 97 % of the vaccinated patients would recommend vaccination to other IBD patients.

3) PRE-OPERATIVE CARE

Improved outcomes for patients undergoing colectomy for acute severe inflammatory colitis by adopting a multi-disciplinary care bundle

BOLDOVJAKOVA D, ET AL. J GASTROINTEST SURG. 2022 JAN;26(1):218-220, DOI: 10.1007/S11605-021-05082-2.

This single-center retrospective observational study, compare the risk of complication after colectomy due to colitis before and after they started discussing the patients at a MDT conference (1 April 2014).

296 patients were identified, 113 patients of these (38.2 %) experienced a complication after surgery. The overall complication rate improved over time (p = 0.023). Patients treated after the initiation of the MDT conference had reduced complication rates (33.7 versus 44.6 %, p = 0.045). In multivariable analysis, increasing age (1.023 OR; 95 % CI 1.004-1.041) and procedure performed before MDT bundle (3.1 OR; 95 % CI 1.689-5.723) were independent predictors for post-operative complications.

REFLECTION

The study shows that patients undergoing acute colectomy benefit from a closer cooperation between gastroenterologists and surgeons, i.e. a MDT conference. They did not analyze what was discussed/decided at the MDT conferencee.
Personally, I think the conferences are of great importance, even more for IBD patients undergoing elective surgery.

4) PRE-OPERATIVE CARE

Effectiveness of a Telephone-Based Motivational Intervention for Smoking Cessation in Patients With Crohn Disease: A Randomized, Open-Label, Controlled Clinical Trial.

NAVARRO CORREAL E, ET AL. GASTROENTEROL NURS. 2021 NOV-DEC 01;44(6):418-425. DOI: 10.1097/SGA.0000000000000572.

Smoking CD patients above 18 years were randomized between motivation intervention based on the 5 R's model (relevance, risks, rewards, roadblocks, and repetition) delivered by specialized inflammatory bowel disease nurses every 3 months over a 1-year period and regular follow-up.

144 patients (72 per group) were included (50 % women, median age 40 years). In median 10 cigarettes were smoked per day (range = 1–40) and they had been smoking for a median of 22 years (range = 1–51). Motivation to quit was assessed to be low in 73 patients, moderate in 39 patients, and high in 32 patients (Richmond test).

14 patients (20.9 %) in the intervention group and 9 patients (13.2 %) among controls stopped smoking at the end of the study (ns between groups).

The authors conclude that the motivational intervention was associated with a trend towards smoke cessation and that the tool can be useful to help patients stop smoking.

REFLECTION

I think the results of this Spanish study are terrifying. They interviewed 283 CD patients, of which 150 was smoking. 148 accepted the study. 144 were not willing to stop smoking and this group was the study base. 79 % in the intervention group and 87 % in the control group were still smoking at the end of the study.

If the patients are referred for surgery, smoking cessation is even more important since the risk for complications can be dramatically reduced if they stop smoking (Lindström D, et al. Ann Surg 2008).

5) SURGICAL TECHNIQUE

Mesenteric Excision and Exclusion for Ileocolic Crohn's Disease: Feasibility and Safety of an Innovative, Combined Surgical Approach With Extended Mesenteric Excision and Kono-S Anastomosis.

HOLUBAR SD, ET AL. DIS COLON RECTUM. 2022 JAN 1;65(1):E5-E13. DOI: 10.1097/DCR.0000000000002287

In ileocolic resection for Crohn's disease the mesentery is traditionally transected close to the bowel and a wide anastomosis is performed, often stapled. The mesentery is an immune active organ that has recently been suggested to affect the CD pathology. It has been suggested that the mesentery should be removed to prevent recurrence of CD. A new configuration of anastomosis, the Kono-S anastomosis has

also been suggested to benefit CD patients.

In this single center report, 22 patients with ileocecal CD underwent mesenteric exclusion and 19 of these Kono-S anastomosis (3 received a stoma). 30-day outcomes were reported. A video of the surgical technique is presented.

Of the 22 patients, all had strictures, 13 (59 %) had fistulas, 18 (81%) were on biologics, and 6 (27 %) had previous ileocolic resection. 16 (72 %) underwent laparoscopic procedures, a mesenteric defect was closed in 19 (86 %), omental flaps were fashioned in 17 (77 %), and 3 (14 %) patients were diverted. Median operative time was 175 minutes. Median postoperative stay was 4 days. At 30 days, there were 2 readmissions for reintervention: 1 seton placement and 1 percutaneous drainage of a sterile collection. There were no cases of intra-abdominal sepsis or anastomotic leak.

The authors conclude that mesenteric excision and exclusion "represents an innovative, progressive, and promising approach that appears to be highly feasible and safe" and, as always, more studies are needed.

REFLECTION

For a surgeon, it is always intriguing with new techniques. The Kono-S anastomosis has been discussed a few years. It is a combination of stapled and hand-sewn anastomosis. In the present study only short time results were presented. Previously, a systematic review (Alshantti A, et al. Colorectal Dis. 2021) including 896 patients found that Kono-S anastomosis was associated with fewer surgical anastomotic recurrences then conventional technique (0 %–3.4 % vs 15 %–24.4 %). Promising results have been described after mesenteric exclusion, but the data is limited. Maybe time for a multi-center trial?

6) OUTCOMES AFTER SURGERY

Systematic Review and Meta-analysis of Outcomes After Ileal Pouch-anal Anastomosis in Primary Sclerosing Cholangitis and Ulcerative Colitis.

BARNES EL, ET AL. J CROHNS COLITIS. 2021 AUG 2;15(8):1272-1278. DOI: 10.1093/ECCO-JCC/JJAB025.

It is controversial to recommend an ileal pouch-anal anastomosis (IPAA) to patients with primary sclerosing cholangitis and ulcerative colitis (PSC-UC) who require colectomy since the risk of pouchitis is increased.
This systematic review identified 11 studies comparing the risk for pouchitis and 6 studies comparing pouch failure among patients with PSC-UC and UC alone.

A total of 4108 patients underwent an ileal pouch-anal anastomosis after proctocolectomy for UC. 3799 (92 %) had UC alone and 309 (8 %) had PSC-UC.
Patients with PSC-UC compared with UC alone were significantly more likely to develop any pouchitis (63 % vs 30 %, OR 4.21, 95 % CI 2.86–6.18), chronic pouchitis (47 % vs 15 %, OR 6.37, 95 % CI 3.41–11.9), and pouch failure (10 % vs 7 %, OR 1.85, 95 % CI 1.08–3.17).
The authors Concluded that pouchitis and pouch failure is more common in patients with PSC-UC.

REFLECTION

The risk for pouchitis is high in patients with PSC-UC, almost half of the patients had chronic pouchitis, while the risk for pouch failure was only slightly increased. The risk for cancer was not analyzed in the study but commented in the discussion. The cancer risk after IRA is higher in PSC-UC than UC patients (9.3 vs 4.9 %, Nordenvall et al. Inflamm Bowel Dis 2018) while cancer development in an IAPP has been found in 3.3 % after 20 years (neoplasia in 6.9 %, Derikx et al. Gastroenterology 2014).

We accept PSC-UC patients for pouch surgery but do not recommend IPAA to patients with a previous history of dysplasia or cancer. It is of major importance to inform PSC-UC patients of the increased risk for malfunction as well as cancer.

7) FERTILITY AFTER SURGERY

Assisted Reproductive Technology in Crohn's Disease and Ulcerative Colitis: A Systematic Review and Meta-Analysis.

LAUBE R, ET AL. AM J GASTROENTEROL. 2021 OCT 25. DOI:10.14309/AJG.0000000000001537.

The primary endpoint of this systematic review (11 studies) and meta-analysis (4 studies) by Laube et al. was pregnancy and live birth rate per cycle of Assisted Reproductive Technology (ART).

Compared with the general population, patients with CD had similar pregnancy rates but they had reduced live birth rates per cycle ART (OR=0.67, 95 % CI: 0.53-0.85). Dividing the CD patients between patients with/without surgery, the reduced live birth rate was only seen in patients who had undergone surgery for CD.

Women with UC have similar chance of pregnancy and living child per cycle ART as the general population. The sub-group of patients with pouch failure had lower chance of living birth after IVF (OR=0.36, 95 % CI: 0.14-0.92).

The authors conclude that ART success rate is similar in women with UC and medically treated CD compared to the general population. Reduced ART success was seen in surgically treated CD patients and patients with pouch failure. And they also conclude that ART is safe in IBD patients.

REFLECTION

I find it difficult to inform about fertility and ART since there are many different measures, but I find this article is useful for the ART part. The authors suggest early referring of patients with CD to a fertility clinic if they fail to conceive naturally and wait with IAPP-surgery until after completion of childbearing.
We know that fertility is markedly reduced after open IAPP-surgery. All IAPPs included were performed with open technique. This negative effect seems to be smaller after laparoscopic surgery (only data from small studies). Many women want to undergo reconstruction before childbearing, and we hope the problem will be less marked in the future since most IBD surgeries are performed minimally invasive today.

8) LONG-TERM RESULTS WITH OR WITHOUT SURGERY

Probability of Stoma in Incident Patients With Crohn's Disease in Sweden 2003-2019: A Population-based Study.

EVERHOV ÅH, ET AL. INFLAMM BOWEL DIS. 2021 OCT 7:IZAB245. DOI: 10.1093/IBD/IZAB245.

The authors have divided 18.815 Swedish CD patients after the year of diagnosis (2003–2006, 2007–2010, 2011–2014) and anlysed the use of anti-TNF, surgery and stoma closure over time.

In total, 3.5 % of patients received a stoma. The cumulative incidence of having a stoma after 5 years was 2.5 % with no difference over time. The incidence was higher in patients older at diagnosis (above 60 years compared with 17–39 years) and with perianal disease.

Permanent stoma was defined when the stoma was still left after 2 years. The risk for a permanent stoma was higher in patients aged >40 years at diagnosis, perianal disease and anti-TNF treatment. Within 5 years of diagnosis, 0.8 % had a permanent stoma. Only 0.05 % had undergone proctectomy.

REFLECTION

The authors conclude that the risk for a stoma is unaltered albeit increased anti-TNF use. However, the risk for stoma was lower than in previously described (2.5 % after 5 years) and the risk for a permanent stoma 5 years after diagnosis was only 0.8 %. I think this study give us a good perspective of the disease.

9) LONG TERM RESULTS WITH OR WITHOUT SURGERY

Surgery, cancer and mortality among patients with ulcerative colitis diagnosed 1962–1987 and followed until 2017 in a Danish population-based inception cohort.

BURISCH J, ET AL. ALIMENT PHARMACOL THER. 2022 FEB;55(3):339-349, DOI: 10.1111/APT.16677

This Danish study used long-term data to anlyse the natural disease course of unselected patients with UC. All incident patients with UC diagnosed between 1962 and 1987 in Copenhagen County, Denmark were included in a population-based cohort. Information about IBD-related surgeries, cancers and mortality from 1962 to 1987 was retrieved from the registry and from the Danish National Patient Registry, Cancer Registry, and Register of Causes of Death during 1988–2017. Each patient was matched with up to 50 individuals from the general population.

In total, 1161 patients were followed for a median of 34 years. The median age at diagnosis was 33 years. The cumulative probability of colectomy after 10, 20, 30, 40 and 50 years was 22 %, 27 %, 31 %, 34 %, and ▶

40 %, respectively. The risk of cancer in the small intestine (RR: 6.26, 95 % CI: 2.25-17.47), colon (RR:1.45, 95 % CI:1.02-2.08), rectum (RR:1.87, 95 % CI: 1.19-2.95) and anus (RR: 4.27, 95 % CI: 1.34-13.65) was higher than among controls, as was cancer of the skin, pancreas (RR: 2.09, 95 % CI: 1.25-3.49) and thyroid (RR: 4.23, 1.72-10.40). All-cause mortality was lower compared to controls (adjusted RR: 0.90, 95 % CI: 0.82-0.99).

REFLECTION

In this population-based cohort of Danish UC patients 40 % underwent colectomy within 50 years of diagnosis. The risk of intestinal and several extra-intestinal cancers was increased. However, the overall mortality was not higher than in the background population. The authors write “our findings high-light the need for long-term follow-up…”.

10) OLD PATIENTS WITH IBD

High Rates of Mortality in Geriatric Patients Admitted for Inflammatory Bowel Disease Management

SCHWARTZ J, ET AL. J CLIN GASTROENTEROL. 2022 JAN 1;56(1):E20-E26. DOI: 10.1097/MCG.0000000000001458

Data from the National Inpatient Sample (2016–2017), on 259.250 admissions with IBD or IBD related complications (as primary or secondary diagnosis) was used to compare risk of mortality in patients younger or older than 65 years. Patients aged over 65 years were defined as geriatric. In total, 30 % of UC and 20 % of CD admissions were geriatric.

Mortality in patients >65 was 3.6 % for non-IBD patients, 3.9 % for CD patients and 5 % for UC patient.

Mortality in patients <65 years was 1.1 % in non-IBD patients, 0.5 % in CD patients and 1 % in UC patients.

After adjustment (for comorbidities, admission type, hospital type, inpatient surgery, and IBD subtype), age above 65 years was associated with higher odds of mortality for CD patients (OR: 3.47, 95 % CI: 2.72-4.44) and UC patients (OR: 2.75, 95 % CI: 2.16-3.49).

Cause of death was approximately 80 % infectious in both CD and UC in all groups.

REFLECTION

The mean age in the younger group was 40.4 years and in the older 74.3 and that older patients do worse is not surprising. In the study, the cause of death was difficult to understand. Unfortunately, being an US study, more focus was placed on ethnicity and medical assurance than on patient characteristics, medical treatment and surgery.