Crohn’s Disease - when to operate?

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**INTRODUCTION**

Crohn’s disease is a chronic bowel condition, which can present as a number of different clinical and pathological presentations, depending on localization and activity of the inflammatory process. The aetiology of the disease has not been explained. In each case the treatment should be individually tailored depending on the type of the changes. The indications for surgical intervention are continuous bleedings, recurrent ileus, perforation of the intestine, abscesses, fistulas, failure of pharmacological treatment, resistance to steroids and steroid dependence. In case of the mild type of the disease with few symptoms pharmacological treatment is the right choice. In case of the mild type of the disease with few symptoms pharmacological treatment is the right choice process. In malignant form of Crohn’s disease lack of improvement after 7-10 days of intensive treatment is generally accepted indication for surgical treatment. Fulminant form of the disease is still a clear-cut indication for immediate surgical intervention. Decision on surgical intervention is more difficult and controversial when patient presents with series of subileus recurrences subsiding after conservative treatment. Patients with stenotic form of Crohn’s disease usually require multiple operations most of which are bowel resections. Patients with stenotic form of Crohn’s disease usually require multiple operations most of which are bowel resections therapy. External and internal asymptomatic fistulas should be treated conservatively. The timing of surgical treatment is essential in Crohn’s disease however the prevention from recurrences is also fundamental. It is well proved that preventive administration of 5-ASA (especially mesalazine) and metronidazol can reduce the risk of early recurrences after surgery.

Key words: Chron, disease
and improving quality of life with minimalization of the early and late side effects. There are no accepted standards of treatment; we can speak of some indications what pictures that the area of "unknown" in Crohn's disease is still broad.

Generally the first line of therapy is combination of salicylate (5-ASA), metronidazol, ciprofloxacin, steroids and immunomodulation. 20-year follow up shows that surgical intervention is necessary in up to 80% of patients despite pharmacological treatment. 16 The surgical intervention is most frequent during the first 3 years from the onset of disease and reaches 24-45% of all patients. 10-14 Risk factors influencing the necessity for the first surgical intervention are cigarette smoking, small intestine presentation and disease progression with concomitant abdominal pain, nausea and vomiting. The need for early surgical treatment is significantly less frequent in patients with colon presentation and in those who underwent 6 month 5-ASA therapy as an initial treatment. 11 The indications for surgical intervention are continuous bleedings, recurrent ileus, perforation of the intestine, abscesses, fistulas, failure of pharmacological treatment, resistance to steroids and steroid dependence.

Surgical treatment of Crohn's disease is still very controversial. One of the main problems is the right timing of the procedure. Surgeon should be aware of many factors, which can influence recurrences and number of complications. The type of the procedure and its timing should be dependent on the disease presentation and localization, on clinical presentation and its severity. All parts of the intestinal tract can be affected by the inflammation including duodenum, stomach and esophagus. Small intestine, colon and rectum are the most frequently affected parts of the GI tract. Typical localization of inflammatory changes in Crohn's disease is the distal part of ileum and cecum. The changes can be restricted to a single localization but also can be present in multiple sites. Crohn's disease has been divided into three subtypes: first without strictures, fistulas and perforation; second with strictures and the third one with abscesses and fistulas. The division has a role in prognosis, in predicting type of complication and in time and type of the possible surgical intervention.

The first type of the disease rarely requires surgery.

The right timing of the surgical procedure is very important factor. Most surgeons face the same problem of choice between the most rational and most proper procedure at the time most optimal for the patient. All the above mentioned factors have to be considered before making the decision of the surgery.

Crohn's disease of the first type without strictures, perforations and fistulas least frequently requires operations as well as reoperations. Depending on the severity of symptoms it can have different clinical presentation: mild, moderate, severe to fulminate. The severity of symptoms can change during the disease.

In case of the mild type of the disease with few symptoms pharmacological treatment is the right choice. The controversy arises when asymptomatic inflammatory tumor is found. It is generally accepted that wide spectrum antibiotics and parenteral steroids should be administered. If symptoms of ileus are absent this treatment can diminish the tumor growth. We have to remember that, although rare, inflammatory changes can be the base for neoplastic growth. We think that after course of pharmacotherapy and reduction of tumor size the surgical treatment should be taken into consideration. Surgery is indicated when we do not observe reduction in tumor size or its growth regardless pharmacological therapy.

According to American Gastroenterological Association in the mild type of the disease pharmacotherapy is the treatment of choice but surgical intervention should be alternatively considered. Mild type of the Crohn's disease normally is characterized by the periods of remissions and exacerbation's which withdraw after intense pharmacological treatment. The times of exacerbations are extremely disturbing for the patient, usually cause limitation of physical activity, quality of life, have negative impact on mental condition and unable normal work activity. For those reasons the surgery should be considered in some cases. Partial resection of the small bowel and cecum is the most frequent surgical procedure performed in Crohn's disease both conventionally and laparoscopically. Crohn's disease is characterized by the recurrences or more accurately escalation of the inactive process. Recurrences after surgery (in all forms of the disease) occur in 50-84% cases and the rate of the reoperations ranges from 32 to 65% 20,21. Frequency of reoperations is substantially lower in moderate form of the disease (without stenoses, fistulas or perforations). Necessity of reoperation is statistically significant only in forms with stenoses, fistulas or perforations. Average time before reoperation in the group with prerogative form of the disease was 1,7 years, comparing to 1,3 years in the group without perforation or fistulas. Patients with moderate form of the disease without abdominal complications have a chance to avoid symptoms of Crohn's disease for a long time after surgical treatment, or in some cases for the rest of life. They have a chance to return to normal personal and professional life. After curative surgery most patients regret that they had not decided to undergo operation earlier, which would have released them from the symptoms. The doctor together with patient educated in perspectives of treatment, should decide about surgical intervention together. They should consider all advantages and disadvantages of the surgery. Decision should be very fast in steroid - resistant or steroid - dependent patients, when remission periods are very short.

In malignant form of Crohn's disease lack of improvement after 7-10 days of intensive treatment is generally accepted indication for surgical treatment. Despite effective treatment of the recurrences followed by the remission, surgical treatment in the malignant form of the disease should also be considered.

Fulminant form of the disease is still a clear-cut indication for immediate surgical intervention.

Crohn's disease with strong fibrosis and narrowing leading to ileus or subileus is treated surgically. Ileus can occur not only as the effect of massive bowel wall fibro-
sis, but also can be caused by the adhesions. Of course in case of obstructing ileus surgical treatment is imminent. Decision on surgical intervention is more difficult and controversial when patient presents with series of subileus recurrences subsiding after conservative treatment. Bowel stenoses are usually multifocal and can occur in many new sites during the disease. Therefore frequent recurrences after surgical treatment are often and sometimes require further, sometimes multiple surgical procedures.

Consecutive resections increase the risk of short bowel syndrome. Recurrences do not depend on microscopic presence in the bowel margins. That gives us the possibility to perform minimal surgery like stricturoplasty. On strictures up to 8 cm long, we perform Heinecke – Mikulicz stricturoplasty. Strictures of 8-20 cm should be treated by Finney operation. If the stricture exceeds 20 cm resection with primary anastomosis should take place. The best procedure to maintain good bowel function is Heinecke – Mikulicz procedure. After segmental resection, wide stapled anastomosis can prevent local recurrences.

We need to remember that risk of recurrence is significantly higher in the small intestine.

Patients with stenotic form of Crohn’s disease usually require multiple operations most of which are bowel resections. It seems that the delay in the first, as well as next surgical interventions is the good strategy in that form of the disease. It is only possible if consecutive subileus recurrences diminish after conservative treatment. Operation should be reserved for patients with severe cases of recurrent subileus, patients with significantly decreased quality of life, affecting their mental condition alone with social and professional life. Patient should be informed about high risk of recurrence (anastomotic or other location stenosis). Performing stricturoplasty, we need to remember about risk of adenocarcinoma development in stricturoplasty site. This is especially important in patients with long lasting treatment of Crohn’s disease. Control colonoscopy and/or endoscopic evaluation is necessary. Presence of cancer is immediate indication for the surgery.

Intestine perforation, abscess and fistulas are connected with most severe form of Crohn’s disease. That form is the most frequent indication for the surgical treatment. Bowel perforation with peritonitis is clear-cut indication for surgical intervention. In those cases resection of changed bowel including perforation place is an appropriate procedure. When intraabdominal abscess is found (pain in the abdominal area and hectic fever) the emergency intervention is required. There are suggestions that some abscesses can be treated by the precutaneous drainage under Ultrasound or CT control. Most of intraabdominal abscesses are located between bowel loops therefore precutaneous access is not always possible. In our opinion intraabdominal purulent complications require urgent laparotomy. In case of perforation segmental resection of changed bowel is the treatment of choice. Massive peritoneal cavity lavage and effective drainage is a necessity.

Surgical intervention for the abdominal purulent complications is not questionable but fistulizing Crohn’s disease is more problematic.

Fistulas in Crohn’s disease occur in up to 35% of patients, in which 20% are perianal fistulas. Intrabdominal fistulas present in 5-10% patients. There are three types of intraabdominal fistulae: intestinal, between intestines and vagina, and between intestines and urinary tract (bladder is the most common location). Cutaneous fistulas, including parastratal fistulas although rare can also be present.

Recto – vaginal and perianal fistulas, with changes limited to the rectum are separate group, because of specific symptoms and treatment. It is called perianal location of Crohn’s disease.

Most common intraabdominal fistulas appear between small and large bowel (usually sigmoid colon) rarely between loops of small bowel. Treatment of intraabdominal and intestinal fistulas depend on clinical presentation, symptoms and complications. Conservative treatment with 5 ASA (mesalazine), metronidazole and ciprofloxacin, should always be the first line therapy.

It was proved that therapy with mesalazine leads to fistula closure in 55% of cases. In comparison metronidazole and ciprofloxacin therapy is successful in 50% and 70% respectively. Using a combination of these two antibiotics causes fistula closure in 20% and gives positive response in 85%. In asymptomatic fistulas 5-ASA, metronidazole and ciprofloxacin are the first line of treatment. Although in most cases this treatment is not followed by fistula closure, it helps in symptoms control and improvement of quality of life. It is accepted that steroids shouldn’t be used in fistulizing Crohn’s disease.

Suppurative complications as well as rare enteros-extrapertoneal fistulas are indications to emergency surgery. The exact localization of the fistula has a big therapeutic implications including surgery decision making. High fistulas can cause absorption disturbances including blind loop syndrome and can lead to serious caehexia. In this case the decision about surgery should be considered. The patient presenting with high fistulas should be fed parenterally for at least two weeks. Operation strategy depends on the local changes observed intraoperatively and usually consists of partial resection of involved bowel with entire fistula’s canal.

Operation is also indicated in cases of external fistulas that do not respond to conservative treatment. In course of these fistulas leaking content causes steeping and inflammation of surrounded skin. The operation should be done in cases of peristomal fistulas which are characterized by the high output and may cause inflammation of peristomal skin area. Resection of both stoma and fistula with partial bowel resection usually followed by stoma transposition is the treatment of choice. We have to remember that the operation should be performed during remission of the disease, usually 3-6 months from exacerbation.
Recently, laparoscopic techniques became more accepted surgical procedure of fistulizing Crohn’s disease. This method is successfully used both in primary and secondary operations.24,25,37-41

External and internal asymptomatic fistulas should be treated conservatively. In cases of no response to 5-ASA, metronidazole and ciprofloxacin as well as immunomodulation should be introduced. This therapy leads to good response in 54-65% of patients and to fistula closure in 31-39%.42-46 Allergic skin eruption, fever, acute pancreatitis and leucopenia can be serious adverse effects of drug therapy with immunomodulators. Monoclonal anti-TNF antibody (infliximab) is promising new therapy in fistulizing Crohn’s disease not responding to 5-ASA, antibiotics, and immunomodulators. Successful closure of the fistulas was observed in 24-55% with relatively low risk of adverse drug reactions.47-50 It seems that infliximab should be used as a first line therapy in internal and external asymptomatic fistulas that do not respond to conventional treatment.49

In our opinion, despite proved therapeutical value, methotrexate, cyclosporine A, tacrolimus and should not be used because of their serious adverse drug reactions and toxicity. Using these drugs need further evaluation.

Surgical operation should be considered if conservative fistula treatment is not effective and quality of life is diminished.

The same methods of treatment should be used in cases of urinary tract – intestine fistulas without supplicative complications. Unfortunately in most patients with this type of fistula who were treated surgically, results were not good. It seems that this type of fistulas should not be an indication for the surgical treatment. The only indications are intraabdominal abscess, bowel obstruction, prolonged urinary tract infections and renal dysfunction.

Rectal type of Crohn’s disease is a distinct clinical problem. This type is characterised by perianal fistulas, abscesses and recto-vaginal fistulas. Frequency of perianal fistulas in Crohn’s disease is estimated between 17 and 43%.51 Perianal fistulas are the first and only symptom in 10% of patients.52 We have to remember that most often ulcerative colitis with multiple perianal fistulas is in fact misdiagnosed Crohn’s disease. Perianal fistulas are more frequent in colonic Crohn’s disease.53 In rectal type of Crohn’s disease perianal fistulas occur in 100% of patients.54 Perianal Disease Activity Index (PDAI) is used to estimate the activity of this type of disease. It describes secretion, pain, sexual activity limitations and rate of tissue induration.55,56

Perianal abscess accompanied by severe pain and fever is an indication for the emergency surgery. Wide, simple incision with careful cavity control has to be done in superficially situated abscesses and potential fistula canal should be localized. Incision has to be appropriate for the easy abscess drainage. In some cases setonage is helpful. Deep abscesses despite wide incision require thick rubber drain. In abscesses connected with fistulas, draining threat or rubber should be stretched through the canal and left in place (non cutting seton method).

Surgical treatment of the perianal fistulas should be careful and non-aggressive. Conservative therapy is substantial in rectal type of the disease with active inflammation (5-ASA, metronidazol, ciprofloxacin, immunomodulation), surgery is not recommended. Pharmacological therapy can lead either to complete healing of some of the fistulas or diminishing symptoms. The best time for surgery is 3 to 6 months period from the withdrawal of acute inflammation symptoms. Small and superficial fistulas with no inflammation are treated with simple fistulotomy followed by weekly administration of metronidazole and ciprofloxacin. "Non-cutting seton" drainage with either thread or rubber should be performed in cases of fistulas with severe inflammation. Deep, transsphincteric or suprasphincteric fistulas are the indication to drainage and long lasting therapy with metronidazole and ciprofloxacin. The treatment leads to complete healing of 85% of patients with fistula – complete healing is closing of the fistula.57 Advancement flap method is considered as the alternative procedure in patients with rectal fistulas without inflammation.58,59 In our opinion this way of treatment should not be performed in Crohn’s perianal fistulas. The method has high efficacy (80%) in the treatment of fistulas of another origin however in case of Crohn’s disease it is associated only with 50% of positive outcomes (96). Other authors report up to 74% of completely healed patients.60 The results of the treatment are very divergent therefore we suggest "non-cutting" seton methodology as the most efficient one. This method used in complex and high fistulas diminishes the risk of sphincter damage and consecutive anal incontinence.61,62,63 The technique of advancement flap in Crohn’s disease should be limited only to the treatment of recto-vaginal fistulas. Unhealed or recurrent fistulas are indication for permanent rubber or thread drainage with administration of metronidazole and ciprofloxacin together with immunomodulators (azathioprin or 6-mercaptopurin) with or without infliximab. Infliximab should be given in three doses of 5 mg/kg in week 0, 2 and 6.64 It could be prolonged to 2-4 doses of infliximab every 6-8 weeks. The combination of treatment is associated with the very good response in 86% of patients. In 67% of patients it leads to complete healing.65 Non-responding patients with additional chronic inflammation in the rectum are suitable for temporary stoma for a time necessary to heal the fistula. Patients with severe rectal type of Crohn’s disease with massive inflammation in the rectum, non-healing high output perianal fistulas, acute pain, poor quality of life (personal, sexual and professional) can be treated with abdominal perineal extirpation. Treatment resistant, long lasting fistulas in Crohn’s disease are associated with the risk of development of neoplasia. There are the reports of 40 cases of neoplasia on the base of Crohn’s disease.66 Patient is qualified to abdominal perineal extirpation followed by radio and chemotherapy or to palliative radio and chemotherapy alone depending on progression of the disease. The results of the surgery are generally poor.67 Fistula symptoms which
persist for many years, permanent pain despite of the treatment and hardening of surrounding tissues can suggest the neoplasm in which case careful diagnosis should be performed. The best method is MRI.\(^{101,102}\)

The timing of surgical treatment is essential in Crohn’s disease however the prevention from recurrences is also fundamental. It is well proved that preventive administration of 5-ASA (especially mesalazine) and metronidazol can reduce the risk of early recurrences after surgery.\(^{103}\) Giving up of smoking also diminishes the risk of recurrence.\(^{104}\)

We tried to discuss the problem of the timing of surgical therapy in different types of Crohn’s disease. The question when to operate in Crohn’s disease is still opened and requires more studies in representative groups of patients.

BIBLIOGRAPHY