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### Minimally Invasive Surgical Treatment in Crohn's Disease

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#### 1. Introduction

Crohn's disease is a chronic and idiopathic inflammation that can affect any part of the gastrointestinal tract and the terminal ileum is the most frequently involved site; moreover, the first peak of the disease is between 20 and 30 years of age. Surgery plays a very important role in its management: the lifetime risk of surgery is about 70% – 90% <sup>[1]</sup>, for its complications or failure of medical treatment and the reoperation rate is approximately 40% - 50% within 10-15 years after the first operation <sup>[2]</sup>.

Laparoscopic colorectal surgery began in the early 90's; nowadays the equipment development, the surgeons experience and the results of clinical trials lead to affirm the feasibility and safety of laparoscopic surgery, which should be considered as the first line surgical approach in selected patients. In fact, a less surgical trauma should lead to a better preservation of immune response, better cosmetic result, less post-operative pain and faster return of bowel functionality with faster hospital discharge <sup>[3]</sup>.

#### 2. Primary small bowel Crohn's disease

Several studies, including four randomized trials <sup>[4-7]</sup> and three meta-analyses <sup>[8-10]</sup>, demonstrated the benefits of laparoscopic approach in the surgical path of small bowel Crohn's disease, regarding short-term outcomes like post-operative pain and analgesics use, complication rates, return to normal bowel habitus, hospital stay and cosmesis. For these reasons, laparoscopic procedure in primary Crohn's disease is nowadays worldwide considered the first choice surgical treatment.

Many studies showed laparoscopy is less painful than open surgery and requires less analgesics consumption <sup>[11-15]</sup>.

The reduction of post-operative pain leads to a faster mobilization of patients and to an improvement of pulmonary function <sup>[17]</sup>: these are very important factors to obtain lower rates of general complications <sup>[18]</sup> and a smoother recovery.

Benefits of laparoscopic surgery could include lower morbidity, a significantly faster resumption of bowel function and a shorter hospital stay <sup>[4,6,19-23]</sup>. It is well known that the use of opiate analgesics negatively affects recovery of gastrointestinal function <sup>[24]</sup>: laparoscopic approach, due to both a limited wound extension and tissue handling, leads to

a reduction of post-operative pain, morphine supply and to a quick resolution of paralytic ileus and discharge from hospital, respectively.

Furthermore, laparoscopic surgery improves cosmesis and might induce less adhesions <sup>[25]</sup>: this is very important, because patients are generally young and the reoperations are common.

It has been demonstrated that the introduction of a fast-track perioperative care program, also referred to as enhanced recovery after surgery (*ERAS*) <sup>[26, 27]</sup>, may reduce hospital stay to 2-3 days after open colorectal surgery <sup>[28, 29]</sup>, even if high readmission rates are reported <sup>[28, 30]</sup>. Only few studies have evaluated the role of laparoscopic approach combined to fast-track protocols in enhancing recovery after colorectal surgery, obtaining conflicting results: Basse *et al.* <sup>[31]</sup> found no difference between fast-track patients undergone to laparoscopic or open resection, while King *et al.* <sup>[32]</sup> found a significant reduction of the hospital stay in fast-track patients after laparoscopic surgery. The only randomized, multicentric clinical trial (LAFA-study) <sup>[33]</sup> investigating both surgical techniques (laparoscopic and open) combined with fast-track and standard care demonstrated that the best option is laparoscopic resection embedded in a fast-track care; nevertheless, this study focused on colon cancer, so these results have not yet been validated in patients with inflammatory bowel disease.

The mean conversion rate reported in the current literature is 11,2% and it ranges from 4,8% to 29,2% <sup>[8]</sup>.

As already reported in some studies <sup>[6, 34,35]</sup>, the duration of laparoscopic ileocolic resection's laparoscopic surgery can be very similar to open surgery after completion of the learning curve by the surgical team.

It has been demonstrated the safety of laparoscopic ileocolectomy also in the long-term outcomes; Eshuis and colleagues <sup>[36]</sup> showed no differences with open surgery regarding reoperations for disease recurrence and non-disease related complications.

#### 3. Recurrent small bowel Crohn's disease

While for primary laparoscopic ileocolectomy there are many clinical trials demonstrating short and long-term benefits, in the current literature there are only a few studies investigating the feasibility and safety of laparoscopic resection for recurrent disease <sup>[37-41]</sup>, often considering small sample size. Recently Chaudhray and colleagues <sup>[42]</sup> reported one of the largest series of patients who underwent laparoscopic ileocolonic resection for recurrent Crohn's disease, demonstrating the same benefits observed after primary resection without increased complication rates or delayed discharge. Although longer operating time, conversion rate was similar to that reported after primary resection.

In conclusion, more contributions with larger sample size are needed to go deeper into this topic, but laparoscopic approach in recurrent Crohn's disease should not be avoided in principle, because despite high technical difficulty in expert hands can be feasible, safe and lead to significant advantages in the postoperative time.

#### 4. Crohn's colitis

Terminal ileitis is the most frequent presentation of Crohn's disease and more rarely, in about 30% of cases, patients have a disease affecting the colon with or without rectal involvement.

While for small bowel Crohn's disease laparoscopic technique has been worldwide adopted and its benefits well established, in the present literature only a few studies investigated the role of laparoscopy in the surgical treatment of Crohn's colitis.

The largest series of laparoscopic colectomies for Crohn's disease has been recently reported by Holubar and colleagues <sup>[43]</sup> from the Mayo Clinic: 92 patients underwent mini-invasive colectomies with short postoperative length of stay and low morbidity, confirming previous results obtained by other Authors <sup>[44,45]</sup>. Umanskiy and coworkers <sup>[45]</sup> also demonstrated reduced operative times: this result can be attributed to the high experience reached by the surgeons, but also to a selection bias of the patients due to non-randomized inclusion criteria of the laparoscopic group.

Ultimately, laparoscopic approach is feasible and safe in patients with Crohn's colitis and can improve surgical outcome when performed by experienced hands in selected cases; however, these findings must be supported by more contributions and are not yet validated by randomized-controlled trials.

#### 5. Gastroduodenal Crohn's disease

It is a rare conditions that affect up to 4% of patients with Crohn'disease; it can be an asyntomatic endoscopic finding or a clinical-radiological disease where obstruction is the most frequent presentation. Medical therapy with PPI and steroids or immunosuppressive agents is the current management but sometimes surgery is necessary because of its failure; gastrojejunal bypass and stricturoplasty are the validated surgical options. Because this type of disease and surgical procedures are very uncommon there is lack of experience in the current literature regarding laparoscopic approach in the surgical treatment of gastroduodenal Crohn's disease; in 2008, Shapiro and coworkers from The Mount Sinai Medical Center <sup>[46]</sup> published the first experience of 13 laparoscopic gastrojejunal bypass, reporting less morbidity rates and shorter length of stay than after open surgery.

To date, probably due to the rarity of the disease and limited number of operations, no more clinical trials supported these findings and no certain conclusions about benefits of laparoscopic procedures in gastroduodenal Crohn's disease can be drawn.

#### 6. New technical aspects

#### Single-incision laparoscopic surgery

Single-incision laparoscopic surgery was born in the beginning of the Nineties when the first appendectomy and cholecystectomy were performed with the aim of minimizing the surgical incisions and morbidity rates, improving cosmesis and short term outcomes respect to standard laparoscopic procedures. However, this technique developed slowly and only in the last years it has been kept in attention by the surgeons and started to be applied to the main operations of general, urologic and gynaecologic surgery. Recently has been published the initial experience of single-incision laparoscopic segmental colectomy and ileocolic resection for Crohn's disease <sup>[47,48]</sup>, with longer operative time but similar morbidity rates and length of stay compared to laparoscopic assisted procedures. Single-incision laparoscopic surgeons after completion of an additional learning curve, and must be validated by further clinical trial.

#### Laparoscopic resection with transcolonic specimen extraction

Eshuis and colleagues <sup>[49]</sup> reported a series of ten patients affected by Crohn's disease who underwent to entirely laparoscopic ileocolic resection with endoscopic transcolonic specimen removal. The procedure was possible only for small inflammatory mass (<7-8 cm) and needed longer operative time; infectious complications were high with 2 intraabdominal abscesses and patients did not perceived benefits in terms of body image respect to conventional laparoscopic surgery. Thus, based on these findings, benefits of laparoscopic resection followed by endoscopic transcolonic specimen extraction are unclear and the technique doesn't seem as safe as conventional laparoscopic surgery.

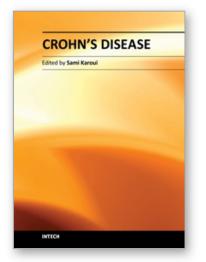
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In this book, several important points regarding Crohn's disease are discussed. In the first section, we focus on etiopathogeny of Crohn's disease and the recent advances in our overall understanding of the disease - specifically, the role of the gut epithelium, alterations of the epithelial crypts, and the roles of the different cytokines in the pathophysiology of Crohn's disease. In the second section, a diagnosis of Crohn's disease is discussed. Another particular area of focus is in the diagnosis of intestinal tuberculosis, and the role of mycobacterium avium in Crohn's disease. In the third and final section, the management of Crohn's disease is discussed, with a focus on recent evidence-based medicine recommendations.

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