

TOPIC HIGHLIGHT

Javier P Gisbert, Professor; Fernando Gomollón, Dr., MD, PhD, Series Editors

Timing of surgery in Crohn's disease: A key issue in the management

Rafael Alós, Joaquín Hinojosa

Rafael Alós, Servicio de Cirugía General, Unidad de Coloproctología, Hospital de Sagunto, Valencia, Spain
Joaquín Hinojosa, Unidad de Digestivo, Servicio de Medicina Interna, Hospital de Sagunto, Valencia, Spain

Author contributions: Alós R and Hinojosa J contributed equally to this work.

Correspondence to: Rafael Alós, Servicio de Cirugía General, Unidad de Coloproctología, Hospital de Sagunto, Valencia, Spain. alos_raf@gva.es

Telephone: +34-96-2659414 Fax: +34-96-2659420

Received: August 18, 2008 Revised: August 26, 2008

Accepted: September 3, 2008

Published online: September 28, 2008

Abstract

The timing of the decision for operation in Crohn's disease is based on an evaluation of the several factors such as the failure of medical treatment, complications due to the Crohn's disease or to the pharmacological therapy, development of dysplasia or cancer and growth retardation. A complete evaluation of these factors should result in operation timed to the patient's best advantage, achieving maximal relief of symptoms with improvement of quality of life. Given the complexity and heterogeneity of the disease and the different options for treatment, is difficult to systematize when the optimal moment for the surgery is arrived. A very important factor in the management of Crohn's disease is the multidisciplinary approach and the patient preference should be a significant factor in determining the choice of therapy. The surgery should be considered such another option in the sequential treatment of Crohn's disease. We have analyzed the factors that are involved in the decision taking of the surgical treatment regarding to the experience and the published literature. When did the medical therapy fail? when is the appropriate moment to operate on the patient? Or which complications of Crohn's disease need a surgery? These are some of the questions we will try to answer.

© 2008 The WJG Press. All rights reserved.

Key words: Crohn's disease; Surgical treatment; Medical therapy

Alós R, Hinojosa J. Timing of surgery in Crohn's disease: A

key issue in the management. *World J Gastroenterol* 2008; 14(36): 5532-5539 Available from: URL: <http://www.wjgnet.com/1007-9327/14/5532.asp> DOI: <http://dx.doi.org/10.3748/wjg.14.5532>

INTRODUCTION

Over fifty years ago, the introduction of corticosteroids in management of active inflammatory bowel disease meant a radical shift in patient management, both from the medical and the surgical standpoints^[1]. Steroids brought about a drop in mortality rates and reduced the need of surgery in flare-ups^[2]. Some forty years later another outstanding leap forward took place in terms of patient management with the introduction of biological therapies^[2,3]. However, despite these advances, it is estimated that approximately 80% of patients with Crohn's disease (CD) will require surgery at some point during their lifetime, especially when the disease is located in the ileocecal region^[4]. In general, the indication for surgery in CD depends on a number of factors-complications, clinical course, relapse and location. Broadly speaking we could say that surgery is timely in any of the following situations: (a) failure of medical treatment, (b) onset of specific complications related to the disease or to pharmacological treatment, (c) dysplasia or cancer and (d) stagnated or retarded growth in children. In some cases it is fairly straightforward to decide when is the best time for surgery- free perforation or abdominal fistula, for instance. However, CD invariably poses a genuine challenge to the team treating the patient. The broad clinical heterogeneity of the disease, the various complications that arise and evolutionary possibilities are all so diverse that it is hard to generalise or adopt a systematic approach when it comes to determining when to operate. Each case should be assessed individually and that is why it is vital to have multidisciplinary teams involved in decision-making together with patients. With these teams it is still possible to improve outcomes^[5], because all the physicians involved have common goals in mind, namely to avoid diagnostic delays, to establish the ideal moment for surgery, to attain the best possible pre-operative conditions and to optimise medical-surgical outcomes; given that this is a chronic disease affecting young

	3 Surgery	Maintenance
	2 Infiximab/Adalimumab	Infiximab/Adalimumab 6-MP/AZA Aminosalicylates?
1	Enteral nutrition (pediatric patients) Oral <i>vs</i> iv corticosteroids or budesonide Oral <i>vs</i> iv antibiotics Aminosalicylates	

Figure 1 Suggested steps in active (left boxes) and inactive (right box) Crohn's disease. 6-MP: 6 Mercaptopurine. AZA: Azathioprine.

patients, medical-surgical management is crucial.

Recent advances in biological therapies have allowed substantial clinical improvements and better monitoring of patients-especially in fistulizing perianal disease-reducing hospitalizations, number of operations and prolonging the time that elapses between diagnosis and surgery^[6]. Colombel *et al*^[7] and Marchal *et al*^[8] suggest that these drugs do not increase post-operative complications in patients with CD, although the same cannot be said in the case of proctocolectomy in ulcerative colitis where the risk of post-op complications is far higher if Infiximab is administered^[9,10]. So, further studies are required to determine the risk of post-operative complications when these drugs are used to treat CD. On the other hand, although a recent meta-analysis of anti-TNF versus placebo did not demonstrate that there is a higher risk of death, tumours or severe infections^[11], one must not forget that biological therapy is not innocuous. The risks/benefits should always be weighed up, bearing in mind that the goal of pharmacological treatment is not to avoid surgery but rather to improve quality of life. If the latter cannot be achieved then surgery will have to be considered as the next step in treatment (Figure 1).

More than half of patients with CD present with affected terminal ileum, with or without extension to the proximal colon, and around 90% will require surgery at some point in their lifetime. Far less frequent-around 10% of all CD patients-are cases presenting with affected proximal areas of the small intestine and the duodenum whereas location in the colon and/or anorectum oscillates around 30%^[12,13]. In these other regions-i.e. not the terminal ileum-the probability of patients requiring surgery is estimated at 60%. According to the classical study by Farmer *et al*^[12] and the more recent review by Bernell *et al*^[4] overall it is estimated that 74% of patients will require initial surgery within the first 13 years from onset of the disease and that around 50% of relapses will require further surgery within the first 10 years of follow-up after the first operation.

Medical treatment failure and/or patients' impaired quality of life are ultimately the reasons leading to surgical treatment. But what do we mean by medical treatment failure? When precisely is it best to conduct surgery? In the face of which complications is it necessary to operate? What other reasons may lead us to decide to opt for surgery? Or, when is quality of life so severely impaired that surgery is called for? These questions remain mooted points in many cases. Answers to these

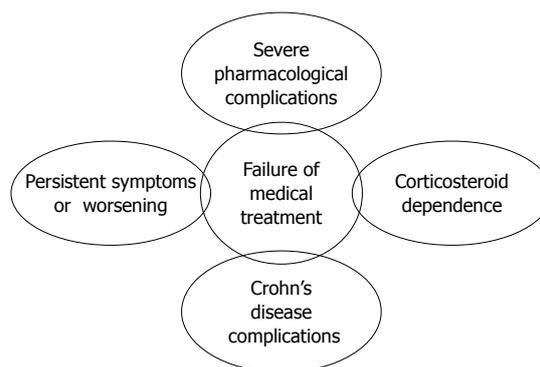


Figure 2 Clinical situations when medical treatment has failed and there is indication for surgery.

questions will depend on the consensus and protocols of multi-disciplinary teams, but patients must always be informed and involved in decision-making.

WHAT DO WE MEAN BY MEDICAL TREATMENT FAILURE?

Once the disease becomes medically untreatable it is necessary to resort to surgery. Failure of medical treatment or "untreatability" of CD is hard to define^[14] and the concept does not bear the same meaning for all physicians or patients. We may consider four scenarios in which surgery is indicated (Figure 2).

(a) Persistence or worsening of symptoms despite correct treatment. In many cases, recognising medical treatment failure on these grounds requires experience and the right clinical judgement. In addition, there are times when it is necessary to consider each patient's individual circumstances since if partial clinical improvement occurs, residual symptoms may or may not be tolerated by patients, in which case subjectivity is a primary factor in deciding to operate. Although biological therapy has meant a remarkable step forward in management of situations involving patients refractory to corticosteroids with mild to severe flare-ups, it is crucial to define response times in order to determine the optimal time for surgery in these particular clinical cases. Non-response to induction with Infiximab or Adalimumab should be considered as therapeutic failure.

(b) Onset of unacceptable drug-related complications and there is no other efficacious medical alternative. This occurs especially with steroids which may trigger severe adverse effects-aseptic femoral necrosis, cataracts, compression-related fractures, *etc.* In rarer cases the same applies with azathioprine or 6-mercaptopurine which may produce medullar aplasia. With the introduction of biological agents, the chances of septic complications or reactivation of latent infections (tuberculosis, viral hepatitis, *etc.*) are high, so extreme caution is necessary^[15]. As to the presence of abdominal or perirectal septic foci these must always be drained before administering Infiximab otherwise severe sepsis may occur^[15].

(c) In cases of steroid-dependence. These drugs

are used to tackle acute crises and not for maintenance purposes; so if after remission of flare-ups the drugs cannot be discontinued after two successive attempts over a six month period, or after three attempts over one year, the case should be considered as untreatable as a result of steroid-dependence. One of the two existing population-based studies included 173 patients with CD, of which 74 (43%) required treatment with steroids and 21 (28%) of these presented with steroid-dependence after a year^[16]. This roughly represents 12% of all patients with CD and the results are similar to those of an earlier trial^[17]. In children, CD is more aggressive and these percentages are higher-more than 60% require steroids and 16% of the total number of patients are steroid-dependent^[17].

(d) Onset of complications associated to the disease that compromise patient's quality of life.

WHEN IS THE OPTIMAL TIME FOR SURGERY?

There is a good deal of controversy surrounding the issue. Those advocating early surgery argue that if medical treatment does not achieve substantial improvement there is no reason to await the onset of a serious, potentially life-threatening complication, or to increase surgery-related risk. Along these lines, one particular study adopted an active surgical approach in 136 patients with mean follow-up of 16.6 years concluding that morbidity and mortality are lower when following this approach, with good functional outcomes and complete remission of symptoms^[18]. Another retrospective study with 74 patients who had undergone various first and subsequent operations for CD between 1975 and 2000 showed that the number of operations increased every 5-year^[19] period, suggesting that the threshold to establish an indication for surgery has dropped with the passing of time (years) in that particular setting. On the other hand, authors critical of early surgery argue that since relapse and re-operation rates are high, the chances of short bowel syndrome are very low. From our point of view, this argument does not hold because since small resections and stricturoplasties are being conducted this syndrome is highly unlikely to occur. In an attempt to identify the factors that increase the probability of surgery in the early stages of CD, Sands *et al*^[20] reached the conclusion that the following have a significant impact: smoking, affection of the small intestine only, nausea and vomiting or abdominal pain as the main form of presentation, neutrophilia and use of steroids within the first six months after diagnosis. In addition, the authors note that the percentage of early interventions is high (20%) and suggest that treatment with rapid action drugs should be initiated in order to change the disease's natural course hence reducing the number of patients requiring surgery. Contrarily, the same authors conclude that when only the colon is affected, blood in faeces, the use of 5-ASA and lymphocytosis are linked to later interventions, although

Table 1 Influencing factors in the choice of optimal time to operate on a patient

Severity of symptoms
Type of symptoms
Failure of medical treatment
Adverse effects of medical therapy
Risk of complications due to Crohn's disease
Established complications
Obvious benefits (or no disadvantages) of surgery
Gastroenterologist
Surgeon
Patient and family

the only independent factor turned out to be affection of the colon alone. More recently, Morimoto *et al*^[21] noted that the only independent risk factors determining whether a patient should be operated are gender (female), and that the disease is located exclusively in the ileum. So, the presence or absence of one or more of the factors described may help us decide how early surgery should be conducted.

On the other hand, the use of drugs that may potentially increase the risk of surgery-related complications should not be an obstacle to surgery if this becomes necessary at some point. In this regard there are few publications addressing steroid-related risk in postoperative CD complications although experience suggests that prolonged preoperative use is an adverse factor in itself. Two recent articles agree in pointing out that there is a higher risk of dehiscences and septic complications if these are administered pre-operatively over more than three months^[22,23]. However, the same authors note that there are other more significant factors that come into play in the onset of post-op septic complications, as is the case with malnourished patients. Regarding treatment with Infliximab, as discussed above, it is highly likely that it has no role in CD post-op complications^[7,8] although further studies are needed. The use of other immunosuppressants does not influence surgery-related complications either^[7].

On the basis of what has been discussed so far, in order to determine the best time for surgery we should assess the severity and type of symptoms, failure of medical treatment, the onset of adverse effects and surgical risk/benefit. All this together will enable gastroenterologists, surgeons and patients to agree on optimal time for surgery with a view to ensuring that the operation will resolve symptoms with no or minimal disadvantages for patients (Table 1). To assess the importance of patients' views in decision-making we note the study by Scott and Hughes^[24] in which they interviewed 70 patients who underwent ileocolic resection to ascertain when surgery should have taken place-earlier, later, or at the time it was conducted. None of the patients declared preference for a later operation, and 77% would have preferred earlier surgery, with a median of at least 12 mo sooner. Almost 100% of interviewees said that the main reason for wanting to bring surgery forward was severity of their symptoms.

Identifying the best time for surgery is not always an easy task. To be as sensible as possible, we should always remember that it is as inappropriate to indicate surgery before having resorted to all the drugs available-selected on the basis of clinical status-as unnecessarily delaying surgery until the onset of a serious complication.

IN THE FACE OF WHICH COMPLICATIONS IS SURGERY REQUIRED?

One of the features of CD is that it may give rise to a number of complications throughout its clinical course (Table 2) that may require surgery.

Intestinal obstruction: This is the most frequent indication for surgery when CD is located in the ileocecal area. This may also occur when CD is located in the jejunoileal area with one or multiple stenoses and, in these cases it may progress with greater severity and a higher probability of large resections^[25]. Approximately 25% of all CD operated patients have undergone surgery due to intestinal obstruction^[1,3] and commonly further interventions are required following a number of sub-occlusion flare-ups, although urgent operations are the exception. If occlusion occurs as a result of inflammatory events with edema in the intestinal wall and there is some response to crisis and maintenance medical therapy then there will be no need for surgery. However, if obstruction is due to fibrosis or reactive scarring changes, an operation is called for once absence of activity has been confirmed. In general terms obstruction is never complete, and responds to conservative treatment with gastric decompression and therapy with fluids and steroids, so surgery can be scheduled in the best possible conditions. In chronic situations, which should be avoided, a large prestenotic dilation of the intestine will appear, palpable as an abdominal tumour, which can cause severe nutrition-related problems.

Although there is no rule of thumb, we may affirm that surgery is indicated when two sub-occlusion flare-ups occur over a period of one year, requiring hospitalisation, or if the steroid treatment prescribed after a crisis cannot be discontinued at three months, or if dosages higher than 15 mg of Prednisone/day are required in the period three to six months following the occlusive crisis^[26]. Delaying surgery in this particular case will lead to patient decline and further complications such as perforation, with an increase in surgery-related morbidity and mortality. In certain cases-single stenosis not larger than 8 cm in length, especially following post-op relapses-if the area is accessible with an endoscope, surgery can be replaced by endoscopic dilation either alone or associated with local steroid infiltration^[27,28].

Abdominal abscess: Abdominal abscess is characterised by the presence of an inflammatory "mass" that always originates in micro-perforations of the intestinal wall; the mass may be an abscess, phlegmon or a combination

Table 2 Complications of Crohn's disease and treatment approaches

Complication	Treatment
Acute intestinal obstruction	Conservative
Recurrent intestinal obstruction	Elective surgery
Abdominal abscess	Percutaneous drainage Total recovery: medical therapy No improvement: urgent surgery Improvement: elective surgery
Abdominal fistula	Enteroenteric Asymptomatic: conservative Symptomatic: elective surgery Enterourologic o enterogynecologic Elective surgery Enterocutaneous Improve nutritional status and elective surgery
Free perforation or massive bleeding	Urgent surgery
Severe acute colitis	Medical therapy No response in 3-5 d: urgent surgery Obvious improvement: medical therapy
Toxic megacolon	Complication of acute colitis: urgent surgery Debut: medical therapy No response in 1-3 days: urgent surgery Response: elective surgery
Perianal disease	Individual treatment and interdisciplinary approach Surgery Failure medical therapy Symptomatic lesions Complications

of both. Excluding perianal disease, this complication is almost exclusive to the ileocecal region. More than a quarter of patients with ileocecal CD need to undergo surgery for this reason. Of these abscesses or phlegmons, 40% are associated with fistulae. In general terms, these are septic patients whose initial treatment, as well as broad spectrum anti-biotherapy and anaerobicides, involved CT or ultrasound-guided percutaneous drainage which allows improving patients' clinical status. The success rate of drainage exceeds 90% and avoids short-term surgery in 50% of patients^[29], whereas those who will ultimately need to undergo an operation will only require single-stage elective surgery, under far more favourable conditions^[30,31]. If even despite drainage, septic status shows no improvement, urgent surgery should be considered. Likewise, surgery is indicated in the event of multiple abscesses for which radiological drainage is not feasible. Normally when an inflammatory "mass" is detected through palpation, it means that the disease has attained such degree of severity that it is very unlikely to respond to medical treatment. Some authors have even reported initial improvement after percutaneous drainage of an abscess in small series of patients, but even so, surgery becomes necessary sooner or later^[32].

Abdominal fistulae: Occur in their majority when CD

is located in the ileocecal region. They may be internal, between neighbouring organs-the most frequent-or external, towards any cutaneous abdominal area-these are almost always post-operative. In the case of a spontaneous enterocutaneous fistula, or one that occurs following abscess drainage, there is consensus in so far that surgery is indicated because closure does not occur spontaneously^[33,34], although some authors report good results in isolated cases with the use of Infliximab^[35]. In the event of malnutrition and sepsis these have to be addressed before the operation since surgery on a fistula of this kind is not an urgent matter. If the fistula is post-operative it must be managed like that of a normal patient. If it occurs prematurely, within the first seven days post-op, in all likelihood it will require surgery; however, if it occurs at a later date but within sixty days one should adopt an expectant approach to treatment,-with enteral or parenteral nutrition-because they do tend to close provided there is no associated obstructive process. A special situation we have had to deal with sometimes, involves CD patients with long course of the disease, presenting with multiple enterocutaneous fistulae and with variable nutritional status, complexity of fistulae, degree of sepsis and food tolerance. In these cases, the decision whether to operate or not has to be assessed individually, on the basis of the factors mentioned.

Internal or enteroenteric fistulae are the most frequent, and alone they are not an indication for surgery, except if they exclude a large segment of the intestine and they are symptomatic, as in ileosigmoid or gastrocolic fistulae^[36,37]. Less frequent are fistulae in the vagina, bladder, urethra and ureter; here the indication is scheduled surgery as the definitive solution^[38].

Free perforation: May occur both in the case of CD in the small intestine or CD in the colon, although it is often associated with toxic colitis or megacolon^[39]. Incidence is low, oscillating between 1%-3%. In this situation, peritonitis occurs, requiring resuscitation and urgent surgery. Some authors have described rupture of an abscess in the abdominal cavity, and obviously this would also require urgent surgery^[40].

Massive bleeding: Occurs in 1%-13% of patients with CD. The first measure is to determine the site where haemorrhaging originates, *via* examination such as endoscopy, arteriography *etc.* The first option is conservative treatment, although probabilities of surgery exceed 60% as shown by the scant series of patients published in the literature^[41,42]. If the bleeding can be stopped it is quite possible that further bleeding will occur, in which case surgery is recommended^[43]. Ideally, it should be possible to ascertain the site of haemorrhaging perioperatively in order to avoid massive resections in this type of patient. To this aim, some authors have used selective arteriography injecting methylene blue tincture to highlight the bleeding intestinal segment^[44].

Severe acute colitis: Here treatment criteria are similar to those for severe acute flare-ups in ulcerative colitis. Active treatment is required with intravenous fluids, thromboembolic prophylaxis, steroids and broad spectrum antibiotics, and considering sequential introduction of Infliximab in the event of steroid-resistance^[45]. Urgent surgery will be conducted in the event of worsening of status in the 24-h period following treatment or within five days if there is no clear recovery^[46]. Joint monitoring-by physicians and surgeons-and the approach outlined above will significantly reduce surgery-related mortality. By analogy with ulcerative colitis, we can affirm that predictive factors for surgery in the severe acute case should be identical to those in CD. Along these lines, Travis *et al*^[47] noted that the presence of gas in three or more loops of the small intestine, and more than eight motions or stools daily, or a PCR above 45 mg/L predicts poor response to medical treatment, whereas Lindgren *et al*^[48] conclude that persistently high body temperature, rectal bleeding or diarrhoea and elevated PCR increases the probability that surgery will be required. The presence of these factors should alert us to the need to conduct stricter surveillance.

Toxic megacolon: Occurs in 4%-6% of all patients with CD in the colon and although it can be controlled initially with medical treatment, in almost all cases delayed surgery should be considered since half of patients will present with a new megacolon flare-up and the other half will be poorly controlled. It occurs more frequently in the case of severe acute flare-up in extensive colitis; in this case, urgent surgery is indicated^[49]. It is rarer as a debut manifestation and if this were the case, intensive medical treatment similar to that applicable to a severe flare-up should be initiated, but if there is no clear improvement, surgery should be indicated after 24-48 h. Immediate action-which reduces mortality rates to 2%-8%^[50]-will prevent the onset of multiple organ dysfunction syndrome and perforation, which yields high mortality rates-close to 40%.

Perianal Crohn's disease: This is sometimes a complex problem which is hard to manage. Treatment must always be designed on a case-by-case basis and symptoms and complications should be treated surgically^[51]. Here the major problems are perianal fistulae and sepsis. In the event of perianal abscess, urgent surgical drainage is always the approach to take. In an attempt to summarise such a complex problem, if the rectum presents no activity or is healthy and the fistulae are straightforward, scheduled fistulotomy is indicated; if they are complex medical treatment is preferable and rarely scheduled surgery for an advanced flap. If the rectum is diseased or there is genuine perianal sepsis, seton drainage appears to be the method favoured by most authors^[51,52]. All septic foci should be drained and drainage seton sutures should be placed along with treatment using Infliximab, since results are better than with Infliximab alone^[53].

In very severe cases that fail to respond to medical treatment, a relatively urgent ileostomy will be needed, in an attempt to control sepsis. Normally, if the rectum is affected and sepsis cannot be controlled, a proctectomy will be required^[54].

WHAT OTHER REASONS MAY LEAD US TO OPT FOR SURGERY?

Dysplasia and cancer. Carcinoma-related risk in colon CD, with long course of the disease, seems to be similar to that associated to ulcerative colitis. A recent meta-analysis suggests that the relative risk of cancer in colon CD is equal to 4.5^[55], so a monitoring programme including colonoscopy and biopsies will be beneficial *a priori*. The same criteria as in ulcerative colitis apply regarding monitoring and indication for prophylactic colectomy. So, surgery is indicated in the event of multi-focal low degree dysplasia, or high degree dysplasia confirmed by two different pathologists^[56]. As with ulcerative colitis, the efficacy of monitoring programmes is controversial^[57]. If CD is located in the ileum the risk of cancer is no higher than that of the normal population^[55]. Under special circumstances risk appears to increase significantly, as is the case of patients diagnosed with CD before the age of 30 and with affected regions of the colon-here the relative risk is 20^[58]. Once the carcinoma is established it may be difficult to determine why it triggers the symptoms that may be confounded with the disease, especially if it located in the ileum. Once diagnosed, surgery is called for following the same oncological principles that apply to any kind of neoplastic tumour. At any event, a significant percentage of cancers are found intraoperatively or during histological examination of the surgical specimen^[26].

Retarded or stagnated growth occurs as a result of the complex interaction between nutritional status, inflammation, severity of the disease and genotype^[59]. In addition, if treatment is based on the continued use of steroids, bone epiphysis will close prematurely. So poorly controlled CD, or that which requires steroid treatment, should be operated on as soon as possible, and in all cases before puberty.

WHEN IS QUALITY OF LIFE SO SEVERELY IMPAIRED THAT SURGERY IS NEEDED?

This question is extremely difficult to address given that no studies have come up with an answer. In addition, the evolution of CD with flare-ups, remissions, and exacerbations means that quality of life (QL) will vary over time. However, measuring QL is a useful tool to gain insight into response to pharmacological treatment, impact of the disease, assessment of healthcare services, contribution of surgical treatment, *etc.* One of the aims of treatment-whether medical or surgical-is to improve

QL of CD patients. A plethora of factors impact QL, such as the fear of relapse, the fear of not enjoying good health and being unable to work, the impact of the disease on body image, infertility, *etc.* Moreover, determining when QL is so severely affected that surgery has been resorted to is also difficult to establish given that each patient may have very different perceptions in terms of how his or her own QL has altered. An organisational change is needed, with the introduction of health education programmes for patients^[60], and dedicated units should be set up to provide comprehensive assistance^[61]. This would improve the quality of healthcare assistance, while optimising healthcare resources^[62]. According to the study conducted by Casellas *et al.*^[63], QL improves in a similar manner both if CD remission is attained *via* medical or surgical treatment, so it may be concluded that the important issue is to achieve remission, regardless of the method of choice.

In some situations, QL is severely affected. For instance, when CD is diffusely located in the small intestine, or when-regardless of location-it leads to nutritional problems or growth impairment, its impact on patients' social life is so great that surgery will have to be considered^[64,65]. In general terms, the factors that patients rank highest as life-limiting factors are: number of motions or stools, appetite and dietary options, sleep, depending on others, mental health and psychosexual morbidity. To assess and measure these factors, a QL questionnaire, specifically designed for inflammatory bowel disease, is used^[66]. The score obtained is closely linked to flare-ups of the disease, so that during remission phases patients refer maximum scores-similar to scores during phases when the disease is under control-whereas greater or lesser activity alters scores, worsening QL proportionally to the magnitude of the flare-up^[63].

CD and ulcerative colitis should not be assessed on the basis of clinical criteria alone. We should use a QL questionnaire to understand patients' genuine status of wellbeing. All factors-both clinical and QL related-taken together will help us decide whether to continue with medical treatment or to indicate surgery.

CONCLUSION

Deciding whether to operate on a patient with CD may be relatively easy although in a variety of cases it can be a difficult call. In these complex cases, an organization based on multi-disciplinary teams, while also bearing in mind patients' opinions, plays an extremely relevant role in order to attain the best possible outcomes. The goal of all those involved is to achieve better quality of life for patients. Hence, surgery should be seen as another treatment option and not as an approach to avoid at all costs. Deciding when is the best time for surgery will essentially depend on a number of factors such as medical "untreatability", symptom severity, types of complications, drug-related adverse effects and adequate risk/benefit assessment of surgery at a given

point in time. An overall view of clinical status along with analysis of each of these factors from an integral standpoint will enable us to adopt the most appropriate decision.

REFERENCES

- 1 **Truelove SC**, Witts LJ. Cortisone in ulcerative colitis: preliminary report on a therapeutic trial. *Br Med J* 1954; **2**: 375-378
- 2 **Rutgeerts PJ**. An historical overview of the treatment of Crohn's disease: why do we need biological therapies? *Rev Gastroenterol Disord* 2004; **4** Suppl 3: S3-S9
- 3 **van Dullemen HM**, van Deventer SJ, Hommes DW, Bijl HA, Jansen J, Tytgat GN, Woody J. Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). *Gastroenterology* 1995; **109**: 129-135
- 4 **Bernell O**, Lapidus A, Hellers G. Risk factors for surgery and recurrence in 907 patients with primary ileocaecal Crohn's disease. *Br J Surg* 2000; **87**: 1697-1701
- 5 **Nicholls J**. The inflammatory bowel disease unit and the multidisciplinary team meeting. *Colorectal Dis* 2007; **9**: 477
- 6 **Lichtenstein GR**, Yan S, Bala M, Blank M, Sands BE. Infliximab maintenance treatment reduces hospitalizations, surgeries, and procedures in fistulizing Crohn's disease. *Gastroenterology* 2005; **128**: 862-869
- 7 **Colombel JF**, Loftus EV Jr, Tremaine WJ, Pemberton JH, Wolff BG, Young-Fadok T, Harmsen WS, Schleck CD, Sandborn WJ. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. *Am J Gastroenterol* 2004; **99**: 878-883
- 8 **Marchal L**, D'Haens G, Van Assche G, Vermeire S, Noman M, Ferrante M, Hiele M, Bueno De Mesquita M, D'Hoore A, Penninckx F, Rutgeerts P. The risk of post-operative complications associated with infliximab therapy for Crohn's disease: a controlled cohort study. *Aliment Pharmacol Ther* 2004; **19**: 749-754
- 9 **Shen B**. Impact of preoperative infliximab use on postoperative infectious complications in ulcerative colitis: the price we have to pay? *Inflamm Bowel Dis* 2008; **14**: 1019-1021
- 10 **Selvasekar CR**, Cima RR, Larson DW, Dozois EJ, Harrington JR, Harmsen WS, Loftus EV Jr, Sandborn WJ, Wolff BG, Pemberton JH. Effect of infliximab on short-term complications in patients undergoing operation for chronic ulcerative colitis. *J Am Coll Surg* 2007; **204**: 956-962; discussion 962-963
- 11 **Peyrin-Biroulet L**, Deltenre P, de Suray N, Branche J, Sandborn WJ, Colombel JF. Efficacy and safety of tumor necrosis factor antagonists in Crohn's disease: meta-analysis of placebo-controlled trials. *Clin Gastroenterol Hepatol* 2008; **6**: 644-653
- 12 **Farmer RG**, Whelan G, Fazio VW. Long-term follow-up of patients with Crohn's disease. Relationship between the clinical pattern and prognosis. *Gastroenterology* 1985; **88**: 1818-1825
- 13 **Michelassi F**, Balestracci T, Chappell R, Block GE. Primary and recurrent Crohn's disease. Experience with 1379 patients. *Ann Surg* 1991; **214**: 230-238; discussion 238-240
- 14 **Hanauer SB**, Meyers S. Management of Crohn's disease in adults. *Am J Gastroenterol* 1997; **92**: 559-566
- 15 **Lopez-San Roman A**, Obrador A, Fortun J, Munoz P, Gassull MA. [Recommendations on tuberculosis and treatment of inflammatory bowel disease with infliximab. 2006 update] *Gastroenterol Hepatol* 2006; **29**: 81-84
- 16 **Faubion WA Jr**, Loftus EV Jr, Harmsen WS, Zinsmeister AR, Sandborn WJ. The natural history of corticosteroid therapy for inflammatory bowel disease: a population-based study. *Gastroenterology* 2001; **121**: 255-260
- 17 **Tung J**, Loftus EV Jr, Freese DK, El-Youssef M, Zinsmeister AR, Melton LJ 3rd, Harmsen WS, Sandborn WJ, Faubion WA Jr. A population-based study of the frequency of corticosteroid resistance and dependence in pediatric patients with Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2006; **12**: 1093-1100
- 18 **Nordgren SR**, Fasth SB, Oresland TO, Hulten LA. Long-term follow-up in Crohn's disease. Mortality, morbidity, and functional status. *Scand J Gastroenterol* 1994; **29**: 1122-1128
- 19 **Edna TH**, Bjerkeset T, Skreden K. Abdominal surgery for Crohn's disease during 30 years in Middle Norway. *Hepatogastroenterology* 2004; **51**: 481-484
- 20 **Sands BE**, Arsenault JE, Rosen MJ, Alsahli M, Bailen L, Banks P, Bensen S, Bousvaros A, Cave D, Cooley JS, Cooper HL, Edwards ST, Farrell RJ, Griffin MJ, Hay DW, John A, Lidofsky S, Olans LB, Peppercorn MA, Rothstein RI, Roy MA, Saletta MJ, Shah SA, Warner AS, Wolf JL, Vecchio J, Winter HS, Zawacki JK. Risk of early surgery for Crohn's disease: implications for early treatment strategies. *Am J Gastroenterol* 2003; **98**: 2712-2718
- 21 **Morimoto N**, Kato J, Kuriyama M, Fujimoto T, Nasu J, Miyaike J, Morita T, Okada H, Suzuki S, Shiode J, Yamamoto H, Sakaguchi K, Shiratori Y. Risk factors and indications for first surgery in Crohn's disease patients. *Hepatogastroenterology* 2007; **54**: 2011-2016
- 22 **Yamamoto T**, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum* 2000; **43**: 1141-1145
- 23 **Alves A**, Panis Y, Bouhnik Y, Pocard M, Vicaut E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum* 2007; **50**: 331-336
- 24 **Scott NA**, Hughes LE. Timing of ileocolonic resection for symptomatic Crohn's disease--the patient's view. *Gut* 1994; **35**: 656-657
- 25 **Higuero T**, Merle C, Thieffn G, Coussinet S, Jolly D, Diebold MD, Zeitoun P, Cadiot G. Jejunoileal Crohn's disease: a case-control study. *Gastroenterol Clin Biol* 2004; **28**: 160-166
- 26 **Lledo S**. Crohn's Disease. Clinical Guides of the Spanish Association of Surgeons. 1th ed. Madrid: Aran Editions SA, 2000: 205-230
- 27 **Ferlitsch A**, Reinisch W, Puspok A, Dejaco C, Schillinger M, Schofl R, Potzi R, Gangl A, Vogelsang H. Safety and efficacy of endoscopic balloon dilation for treatment of Crohn's disease strictures. *Endoscopy* 2006; **38**: 483-487
- 28 **Ajlouni Y**, Iser JH, Gibson PR. Endoscopic balloon dilatation of intestinal strictures in Crohn's disease: safe alternative to surgery. *J Gastroenterol Hepatol* 2007; **22**: 486-490
- 29 **Garcia JC**, Persky SE, Bonis PA, Topazian M. Abscesses in Crohn's disease: outcome of medical versus surgical treatment. *J Clin Gastroenterol* 2001; **32**: 409-412
- 30 **Gervais DA**, Hahn PF, O'Neill MJ, Mueller PR. Percutaneous abscess drainage in Crohn disease: technical success and short- and long-term outcomes during 14 years. *Radiology* 2002; **222**: 645-651
- 31 **Lee H**, Kim YH, Kim JH, Chang DK, Son HJ, Rhee PL, Kim JJ, Paik SW, Rhee JC. Nonsurgical treatment of abdominal or pelvic abscess in consecutive patients with Crohn's disease. *Dig Liver Dis* 2006; **38**: 659-664
- 32 **Neufeld D**, Keidar A, Gutman M, Zissin R. Abdominal wall abscesses in patients with Crohn's disease: clinical outcome. *J Gastrointest Surg* 2006; **10**: 445-449
- 33 **Hill GL**, Bouchier RG, Witney GB. Surgical and metabolic management of patients with external fistulas of the small intestine associated with Crohn's disease. *World J Surg* 1988; **12**: 191-197
- 34 **Poritz LS**, Gagliano GA, McLeod RS, MacRae H, Cohen Z. Surgical management of entero and colocutaneous fistulae in Crohn's disease: 17 year's experience. *Int J Colorectal Dis* 2004; **19**: 481-485; discussion 486
- 35 **Present DH**, Rutgeerts P, Targan S, Hanauer SB, Mayer L,

- van Hogezaand RA, Podolsky DK, Sands BE, Braakman T, DeWoody KL, Schaible TF, van Deventer SJ. Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med* 1999; **340**: 1398-1405
- 36 **McNamara MJ**, Fazio VW, Lavery IC, Weakley FL, Farmer RG. Surgical treatment of enterovesical fistulas in Crohn's disease. *Dis Colon Rectum* 1990; **33**: 271-276
- 37 **Khanna MP**, Gordon PH. Gastrocolic fistulization in Crohn's disease: a case report and a review of the literature. *Can J Surg* 2000; **43**: 53-56
- 38 **Solem CA**, Loftus EV Jr, Tremaine WJ, Pemberton JH, Wolff BG, Sandborn WJ. Fistulas to the urinary system in Crohn's disease: clinical features and outcomes. *Am J Gastroenterol* 2002; **97**: 2300-2305
- 39 **Hurst RD**, Molinari M, Chung TP, Rubin M, Michelassi F. Prospective study of the features, indications, and surgical treatment in 513 consecutive patients affected by Crohn's disease. *Surgery* 1997; **122**: 661-667; discussion 667-668
- 40 **Mowatt JL**, Burnstein MJ. Free perforation of small bowel Crohn's disease: A case report and review. *Can J Gastroenterol* 1993; **7**: 300-302
- 41 **Cirocco WC**, Reilly JC, Rusin LC. Life-threatening hemorrhage and exsanguination from Crohn's disease. Report of four cases. *Dis Colon Rectum* 1995; **38**: 85-95
- 42 **Kostka R**, Lukas M. Massive, life-threatening bleeding in Crohn's disease. *Chir Belg* 2005; **105**: 168-174
- 43 **Veroux M**, Angriman I, Ruffolo C, Barollo M, Buffone A, Madia C, Caglia P, Fiamingo P, D'Amico D. Severe gastrointestinal bleeding in Crohn's disease. *Ann Ital Chir* 2003; **74**: 213-215; discussion 216
- 44 **Remzi FH**, Dietz DW, Unal E, Levitin A, Sands MJ, Fazio VW. Combined use of preoperative provocative angiography and highly selective methylene blue injection to localize an occult small-bowel bleeding site in a patient with Crohn's disease: report of a case. *Dis Colon Rectum* 2003; **46**: 260-263
- 45 **Travis SP**, Stange EF, Lemann M, Oresland T, Chowers Y, Forbes A, D'Haens G, Kitis G, Cortot A, Prantera C, Marteau P, Colombel JF, Gionchetti P, Bouhnik Y, Turet E, Kroesen J, Starlinger M, Mortensen NJ. European evidence based consensus on the diagnosis and management of Crohn's disease: current management. *Gut* 2006; **55** Suppl 1: i16-i35
- 46 **Fazio VW**, Wu JS. Surgical therapy for Crohn's disease of the colon and rectum. *Surg Clin North Am* 1997; **77**: 197-210
- 47 **Travis SP**, Farrant JM, Ricketts C, Nolan DJ, Mortensen NM, Kettlewell MG, Jewell DP. Predicting outcome in severe ulcerative colitis. *Gut* 1996; **38**: 905-910
- 48 **Lindgren SC**, Flood LM, Kilander AF, Lofberg R, Persson TB, Sjodahl RI. Early predictors of glucocorticosteroid treatment failure in severe and moderately severe attacks of ulcerative colitis. *Eur J Gastroenterol Hepatol* 1998; **10**: 831-835
- 49 **Berg DF**, Bahadursingh AM, Kaminski DL, Longo WE. Acute surgical emergencies in inflammatory bowel disease. *Am J Surg* 2002; **184**: 45-51
- 50 **Sheth SG**, LaMont JT. Toxic megacolon. *Lancet* 1998; **351**: 509-513
- 51 **Sandborn WJ**, Fazio VW, Feagan BG, Hanauer SB. AGA technical review on perianal Crohn's disease. *Gastroenterology* 2003; **125**: 1508-1530
- 52 **Caprilli R**, Gassull MA, Escher JC, Moser G, Munkholm P, Forbes A, Hommes DW, Lochs H, Angelucci E, Cocco A, Vucelic B, Hildebrand H, Kolacek S, Riis L, Lukas M, de Franchis R, Hamilton M, Jantschek G, Michetti P, O'Morain C, Anwar MM, Freitas JL, Mouzas IA, Baert F, Mitchell R, Hawkey CJ. European evidence based consensus on the diagnosis and management of Crohn's disease: special situations. *Gut* 2006; **55** Suppl 1: i36-i58
- 53 **Regueiro M**, Mardini H. Treatment of perianal fistulizing Crohn's disease with infliximab alone or as an adjunct to exam under anesthesia with seton placement. *Inflamm Bowel Dis* 2003; **9**: 98-103
- 54 **Regimbeau JM**, Panis Y, Marteau P, Benoist S, Valleur P. Surgical treatment of anoperineal Crohn's disease: can abdominoperineal resection be predicted? *J Am Coll Surg* 1999; **189**: 171-176
- 55 **Canavan C**, Abrams KR, Mayberry J. Meta-analysis: colorectal and small bowel cancer risk in patients with Crohn's disease. *Aliment Pharmacol Ther* 2006; **23**: 1097-1104
- 56 **Zisman TL**, Rubin DT. Colorectal cancer and dysplasia in inflammatory bowel disease. *World J Gastroenterol* 2008; **14**: 2662-2669
- 57 **Eaden JA**, Ward BA, Mayberry JF. How gastroenterologists screen for colonic cancer in ulcerative colitis: an analysis of performance. *Gastrointest Endosc* 2000; **51**: 123-128
- 58 **Ekbom A**, Helmick C, Zack M, Adami HO. Increased risk of large-bowel cancer in Crohn's disease with colonic involvement. *Lancet* 1990; **336**: 357-359
- 59 **Shamir R**, Phillip M, Levine A. Growth retardation in pediatric Crohn's disease: pathogenesis and interventions. *Inflamm Bowel Dis* 2007; **13**: 620-628
- 60 **Waters BM**, Jensen L, Fedorak RN. Effects of formal education for patients with inflammatory bowel disease: a randomized controlled trial. *Can J Gastroenterol* 2005; **19**: 235-244
- 61 **Fontanet G**, Casellas F, Malagelada JR. [The Crohn-Colitis care unit: analysis of the first 3 years of activity] *Gac Sanit* 2004; **18**: 483-485
- 62 **Mawdsley JE**, Irving PM, Makins RJ, Rampton DS. Optimizing quality of outpatient care for patients with inflammatory bowel disease: the importance of specialist clinics. *Eur J Gastroenterol Hepatol* 2006; **18**: 249-253
- 63 **Casellas F**, Lopez-Vivancos J, Badia X, Vilaseca J, Malagelada JR. Influence of inflammatory bowel disease on different dimensions of quality of life. *Eur J Gastroenterol Hepatol* 2001; **13**: 567-572
- 64 **Tan WC**, Allan RN. Diffuse jejunoileitis of Crohn's disease. *Gut* 1993; **34**: 1374-1378
- 65 **Norman K**, Kirchner H, Lochs H, Pirlich M. Malnutrition affects quality of life in gastroenterology patients. *World J Gastroenterol* 2006; **12**: 3380-3385
- 66 **Mitchell A**, Guyatt G, Singer J, Irvine EJ, Goodacre R, Tompkins C, Williams N, Wagner F. Quality of life in patients with inflammatory bowel disease. *J Clin Gastroenterol* 1988; **10**: 306-310

S- Editor Xiao LL E- Editor Ma WH