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Quality of Life in Patients with Ileocecal Crohn's Disease after Surgical Treatment

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ABSTRACT

Introduction: *Ileocecal Crohn's disease is the most frequent presentation and requires surgical treatment in many patients. There is little evidence on the impact of surgery in the quality of life of these patients.*

Material and methods: *A retrospective study, based on a prospective database included all patients operated on electively for ileocecal Crohn's disease during a 30-month period. The primary end-point was postoperative change in quality of life, assessed with two validated questionnaires: Short Form-36 and Inflammatory Bowel Disease Questionnaire, performed before and 4 months after surgery. The morbidity of the procedures was also evaluated.*

Results: *Nineteen patients with a mean age of 34 years (23-72) were included. Eighteen (94.7%) patients underwent a laparoscopic approach, with 2 (11.1%) conversions. Major complications presented in 3 (16%) patients, 2 of whom required reoperation due to anastomotic dehiscence. Patients showed an average improvement of 46% in the parameters assessed by the SF-36 questionnaire ($p<0.0001$) and 81 points ($p<0.0001$) in the values of the IBDQ questionnaire after surgery. The mean follow-up was 16 months (4-30).*

Conclusion: *After resective surgical treatment for ileocecal Crohn's disease patients achieved a significant improvement in their quality of life, with a low percentage of major complications.*

Keywords: *Crohn; Inflammatory Disease; Ileocecal; Surgery; Quality of Life; Morbidity*

INTRODUCTION

Crohn's disease (CD) is a chronic and transmural inflammatory process that can affect any organ of the digestive tract and is characterized by exacerbations and remissions. Its incidence has increased worldwide in recent years.[1] It is more prevalent in developed and recently industrialized countries and its highest frequency is between the second and fourth decade of life.[2,3] CD has a great impact on the quality of life of patients, therefore an early diagnosis, the identification of poor prognostic factors and a treatment that prevents complications and induces a prolonged remission are priority objectives for these patients.[4]

Despite advances in the medical treatment of CD, 30-40% of patients will require surgery at some point in their evolution. Its objectives are to resolve complications, restore health and preserve as much intestine as possible, avoiding permanent ostomies and allowing the patient to return to supportive medical treatment.[5,6]

Two thirds of patients present with ileocecal involvement.[7] Although surgery is associated with the resolution of complications that occur during medical treatment, with an early surgical resection these could be avoided, in addition to reducing the morbidity and mortality of the procedure.[8] Few studies have assessed the impact of different therapeutic modalities on quality of life. The aim of this study is to compare the quality of life of patients operated on for ileocecal CD before and after surgery.

MATERIAL AND METHODS

Study design and population selection

A retrospective analysis of a prospectively prepared database was performed on patients with CD located in the ileocecal region with or without extension to the right colon. All patients operated on electively by the open or laparoscopic approach by a team of surgeons specialized in colorectal pathology, between May 2017 and November 2019 were included. The surgical indication was the presence of a complication (stenosis or fistula). Patients with a diagnosis of CD without ileocecal involvement and those who received non-operative treatment during that period were excluded.

The authors declare the absence of conflicts of interest.

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The diagnosis of CD was made in all cases by associating the clinical and laboratory findings, the imaging and the endoscopy with confirmatory biopsy.

All patients signed an informed consent and the study was approved by the institution's ethics committee.

Variables studied and effect measures

For the preparation of the database, the following data were included: age, gender, classification of patients (Montreal score), 9 preoperative treatment with steroids and/or biological agents, type of surgery and approach, follow-up time and quality of life before surgery and 4 months after surgery measured using two questionnaires:

1. Quality of life questionnaire SF-36 (Short Form-36)[10] validated in Argentina: Form of 36 questions that measure the functioning of 8 items related to the patient's life. The results are measured in percentage and a lower value indicates a worse evaluation of the item by the patient.
2. Quality of life questionnaire IBDQ (Inflammatory Bowel Disease Questionnaire):[11] It consists of 32 questions that assess 4 areas of patient functionality. The total score can range between 32 and 224 points, with a lower score reflecting worse functionality.

In turn, length of hospital stay, postoperative complications stratified according to the Dindo-Clavien classification,[12] duration of surgery and whether or not a primary anastomosis was performed were recorded.

The change in the patients' quality of life was taken as the primary end-point, comparing its assessment before and 4 months after surgery. Postoperative morbidity was analyzed as a secondary end-point.

Statistic analysis

The Wilcoxon test was used to compare the quality of life scores. The Fisher test was used for the comparison of categorical variables, and the Mann Whitney test for numerical variables. A correlation study using the Spearman test was carried out between the two scores used to measure quality of life. A value of $p < 0.05$ was considered significant.

RESULTS

During a 30-month period, 20 patients underwent surgery for ileocecal CD, extended or not to the right colon. One patient had to be eliminated due to the finding of an advanced cecal tumor, dying 5 months later for neoplastic progression.

The main patients´ characteristics are summarized in Table 1.

Of the total of 19 patients, 7 (36.8%) had not received treatment with corticosteroids and/or anti-TNF drugs prior to surgery and surgical treatment was indicated due to the onset of disease complications (stenosis or fistulas).

TABLE 1: CLINICAL CHARACTERISTICS OF PATIENTS.

Variable	n = 19
Age, mean (range)	34 (23-72)
Masculine gender, n (%)	13 (68.4)
Time from diagnosis to surgery: years, mean (range)	8 (1-24)
Montreal classification, n (%)	
A2L1B2	10 (52.6)
A2L1B2p	5 (26.3)
A2L3B2	3 (15.8)
A3L1B2	1 (52.3)
Treatment with biologics and/or corticosteroids, n (%)	12 (63.2)
Type of surgery, n (%)	
Ileocecal resection	16 (84.2)
Right hemicolectomy	3 (15.79)
Laparoscopic approach, n (%)	18 (94.7)
Need for reoperation, n (%)	2 (10.5)
Ostomy, n (%)	5 (26.3)
Surgery time: minutes, mean (range)	120 (80-240)
Postoperative length of stay time: days, mean (range)	7 (4-20)
Follow-up: months, mean (range)	16 (4-30)

Sixteen (84.2%) patients had disease located exclusively in the ileocecal region with a stenosing pattern, for which a resection of the compromised segment was performed. Of these patients, 3 (15.8%) had associated fistulizing disease (2 ileoileal fistulas and 1 ileosigmoid fistula requiring sigmoidectomy). The latter, presented concomitantly three ileal stenoses that required strictureplasties.

In 2 (10.5%) patients operated on for a symptomatic stenosis of the ileocecal anastomosis from a previous surgery, the resection of the right colon was completed. The remainder underwent a right colectomy for associated hepatic flexure stenosis. In 3 (15.8%) patients with poor nutritional status and concomitant steroid therapy, it was

TABLE 2: COMPARISON OF SF36 RESULTS BEFORE AND AFTER SURGERY.

Variable	Pre-surgery Mean (range)	Post-surgery Mean (range)	Delta Mean (range)	P
Physical functioning	60 (30-100)	100 (75-100)	30 (-15-65)	0.006
Physical limitation	0 (0-100)	100 (25-100)	75 (0-100)	0.0001
Bodily pain	25 (10-65)	100 (45-100)	65 (33-90)	0.0001
General health	30 (5-55)	65 (25-100)	35 (-10-95)	0.0002
Vitality	25 (0-80)	75 (20-100)	45 (-5-85)	0.0002
Social functioning	37 (12-87)	87 (0-100)	37 (-25-88)	0.0004
Emotional role	33 (0-100)	100 (0-100)	67 (0-100)	0.0001
Mental health	52 (0-76)	75 (32-100)	36 (-8-84)	0.0002
Reported health transition	25 (0-75)	100 (75-100)	75 (25-100)	0.0001
Total score	35 (10-63)	85 (41-97)	46 (21-78)	0.0001

decided to postpone the reconstruction of the bowel transit for a second surgical procedure.

Eighteen (94.7%) patients were approached laparoscopically, 2 (11.1%) of whom required conversion to open surgery due to a large inflammatory tumor that made it impossible to correctly identify the structures. One patient with multiple antecedents of abdominal surgery was treated conventionally.

Nine (47%) patients presented complications in the postoperative period, although 6 were minor (I and II of the Dindo-Clavien classification).[12] Three patients presented peripheral catheter-related phlebitis, one patient presented a wound infection and two a prolonged ileus. Three (16%) patients had major complications, 2 of which required reoperations due to anastomotic dehiscence. One required pacemaker placement due to an electrophysiological disorder.

The assessment of the quality of life of patients with stoma (primary or secondary to anastomotic dehiscence) was carried out before the reconstruction of the bowel transit.

Tables 2 and 3 show the responses to both questionnaires that assessed quality of life before and after surgery. It can be seen that all parameters had statistically significant improvements in the postoperative period.

The items of the SF-36 questionnaire that registered the greatest changes after surgical treatment were those that reflect the physical limitation suffered by the patients, those referring to bodily pain and the emotional role. Taking into consideration all the parameters contemplated, an average improvement of 46% (p = 0.0001) is reflected.

The responses to the IBDQ questionnaire also showed improvements, especially those related to emotional health. An average difference of 81 points was observed between the questionnaires answered before and after surgery (p = 0.0001), demonstrating its positive impact on the quality of life of patients.

In the multivariate analysis, none of the parameters studied (including the presence of an ostomy) generated statistically significant differences.

Finally, the difference in score reflected in the SF-36 questionnaire showed a significant but moderate correlation (r: 0.6 and p = 0.001) with the difference in the IBDQ questionnaire, which could indicate that despite not measuring the same items the questionnaires are complementary, or that patients do not answer both questionnaires in the same way.

DISCUSSION

The ileocecal region is the most frequently affected by CD, which occurs in up to two-thirds of patients.[7] For those with disease at this location who are unresponsive to conventional medications or are steroid resistant / dependent, in the absence of stenosing/fistulizing disease, anti-TNF medications are the second line of treatment.[13] Even after the advent of anti-TNFs, a third of patients with disease restricted to the ileocecal region require surgery within 5 years of starting treatment, due to resistance to it or complications of the disease (stenosis or fistulas).[14-16] In this series all patients presented complications associated with the disease.

Treatment with second-line drugs has shown good results in terms of organ preservation[17-19] but at a significant cost to the health system, especially due to maintenance therapy and with a significant impact on the quality of life of patients who must undergo infusions at regular intervals.[20,21] It is also observed that up to 30-40% of them will subsequently require surgical intervention at some

TABLE 3: COMPARISON OF IBDQ RESULTS BEFORE AND AFTER SURGERY.

Variable	Pre-surgery	Post-surgery Mean (range)	Delta Mean (range)	P
Gastrointestinal symptoms	31 (16-57)	59 (43-69)	27 (10-47)	1
Emotional health	32 (18-65)	68 (56-78)	34 (5-49)	1
Systemic symptoms	13 (7-31)	30 (22-34)	16 (-2-25)	2
Social functioning	14 (5-33)	31 (27-35)	17 (-2-24)	2
Total score	105 (60-166)	196 (165-212)	81 (19-141)	1

IBDQ: Inflammatory bowel disease questionnaire.

point in the evolution of the disease.

The results of elective surgery for patients with ileocecal CD are satisfactory. Performed laparoscopically, it entails a high degree of patient satisfaction due to the significant improvement in the quality of life sustained over time with low morbidity and rapid return to common the activities.[22-24] Some studies have even reported that up to a 50% of these patients remain asymptomatic and untreated up to 7 years after surgery.[25]

The benefits of the laparoscopic approach have been proven in most surgical procedures today. This principle has also been proven in CD surgery by several authors.[26-29] In our series,[18] (94.7%) patients could be approached in this way.

In one of the few studies that have evaluated the quality of life of patients with ileocecal CD after surgical resection, Wright et al.[23] in 2015 presented the results of resections of all macroscopic disease in 174 patients from 17 hospitals. The indications for surgery were complications of the disease and failure of medical treatment. An ileocecal resection was performed in 133 of these patients and a simultaneous proximal resection was associated in 15. Using the IBDQ and SF-36 questionnaires, they measured the impact on the quality of life of patients after surgery, showing a significant and sustained improvement over time. These findings are consistent with the results reflected in the present study. However, the aforementioned study reports better results in those cases treated with biological drugs in the postoperative period.

In another study, Thirbly et al. in 200122 evaluated the impact on quality of life after surgical treatment in 56 patients with CD with the Health Status Questionnaire-HSQ. In 22, the disease was limited to the small intestine. This study also presented an improvement in the quality of life parameters, even showing that in the medium term these values are similar or higher than those of the general population. Another finding of this study was the negative impact of postoperative recurrences.

Hamon et al.[30] found that the majority of their CE operated patients were able to resume their work activities after an average of 11 weeks and reported a significant improvement in daily performance, which is also consistent with the results of the present study.

Finally, the most important study to date on the quality of life in ileocecal CD involved 143 patients from 29 hospitals in the Netherlands and the United Kingdom. Patients with CD refractory to first-line drugs (corticosteroids, thiopurines or methotrexate) were randomized into 2 groups for 3 months: one group received infliximab and the other group received a laparoscopic ileocecal resection.[31] Quality of life was assessed using the same two questionnaires that we used (IBDQ and SF-36). Other variables evaluated were morbidity of both treatments, time of return to work activities, body image and cosmetic result. One year after entering the study, comparable values were observed in both arms in all the parameters evaluated, concluding that both treatment alternatives are valid and comparable for this type of patient in the first year of follow-up. In a second stage, the same group studied the costs associated with both treatments and found that they are much lower for surgery.[32]

Concluding that resective treatment could be more cost-effective than anti-TNF is a very significant finding today, when these drugs represent a paradigm shift in the treatment of inflammatory bowel disease.

Although our patients underwent surgery due to the failure of second-line treatment, the results regarding quality of life and morbidity have been similar to those previously published by other authors.

CONCLUSION

In this series, just over a third of the patients with ileocecal CD required resective surgical treatment without having previously received corticosteroids and/or anti-TNF drugs due to their onset with complications of the

disease, such as stenosis or fistulas. Most could be resolved laparoscopically.

Surgery showed satisfactory results, with a significant improvement in quality of life and an acceptable rate of major complications.

Considering that a large proportion of patients undergo surgical treatment after failure of second-line therapy and in many cases under more unfavorable clinical conditions, we believe that early surgery could further improve the results observed in this study.

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COMMENT

The medical management of Crohn's disease, given the advent of new drugs that show an improvement in the evolution of the disease, the abuse in their use and the maintenance of these treatment programs over time, leads to that many patients with ileocecal involvement present evolutionary complications of the disease such as stenosis and fistulization of a diseased ileum.

It is essential to agree with the treating medical team (Gastroenterologists and Clinicians) when to carry out surgical treatment in these patients. There is no doubt that when faced with an ileal stenosis, we must reach a surgical resolution. Surgical resection is mandatory for extensive stenosis of the terminal ileum.

The laparoscopic approach allows us to inspect the entire abdominal cavity and reduce the aggression of the abdominal wall.

There is no doubt that it is a practice that should be performed by experienced surgeons, on an elective basis. The dilemma may arise when deciding whether or not to anastomose these patients. The previous medical evaluation (comorbidities and general condition) will help to make this decision.

The most feared complication is anastomotic dehiscence, so it is important to consider the technique and suture elements to perform the anastomosis and, on the other hand, to assess whether in the postoperative period it is appropriate to have an imaging study (e.g., tomography) protocolized, for the early detection of this complication, in order to quickly reach its resolution.

I congratulate the authors for their experience, the quality of the work presented and the results obtained. And I agree, as they conclude in the work, that it is very likely that an early surgery could improve the results even more.

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