

Diffuse jejunoileitis of Crohn's disease

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Abstract

Diffuse jejunoileitis is an uncommon, but important manifestation of Crohn's disease because of the associated high morbidity and challenges in medical management. Despite this there have been no studies of prognosis or management of diffuse jejunoileitis for nearly 20 years. This study analysed the outcome among 34 patients (20 women and 14 men) with diffuse jejunoileitis diagnosed between 1960 and 1991 including clinical features, medical and surgical management, death rates, current status, and prognosis. Diffuse jejunoileitis presents in younger patients (mean age at diagnosis 26.4 years) than those with distal ileal Crohn's disease (mean age at diagnosis 33.3 years). Nearly all presented with clear cut abdominal symptoms including a combination of colicky abdominal pain (91%), weight loss (62%), and diarrhoea (53%). Most patients had severe symptoms reflected by the fact that 77% had been treated with corticosteroids for periods of more than six months at some stage during their follow up. The mean follow up from diagnosis was 16 years. Twenty eight patients (82%) had at least one operation for diffuse jejunoileitis and two thirds of the patients (n=21) required two or more operations. The frequency of surgical intervention was particularly high in the younger patients ($r=0.71$, $p<0.001$). The proportion of patients requiring surgery was highest in the first year after diagnosis. The annual operative rate was 15% for the first 10 years and then it fell to 5.2% in years 11-15, and 2.6% in years 16-20. The data suggest that the disease does burn itself out over time. The increasing use of strictureplasty for short strictures and the minimal use of resection has eliminated problems associated with the short small bowel syndrome. The longterm prognosis of these patients is good. Only two patients died (one of perforation of the jejunum and another of an unrelated bronchogenic carcinoma). After a mean interval from diagnosis of 16 years, 24 of 32 living patients are well and symptom free. Only eight have abdominal symptoms of whom three are receiving corticosteroid treatment and one azathioprine. The combination of anti-inflammatory drugs with the relief of recurrent obstructive symptoms by strictureplasty can together produce a good longterm prognosis in most patients with diffuse jejunoileitis.

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Crohn's disease most commonly affects either the distal ileum or the large intestine. While there is often evidence of diffuse microscopic involvement of the gastrointestinal tract, even in apparently localised disease, extensive macroscopic jejunoileitis is uncommon. The reported inci-

dence of diffuse jejunoileitis among patients with Crohn's disease, first described by Crohn and Yunich¹ varies between 3 to 10%.²⁻⁵

Cooke and Swan⁶ reported a series of 18 Crohn's disease patients presenting with diffuse jejunoileitis between 1944 and 1970 of whom six died; one of cancer of the small intestine, one of bronchogenic carcinoma, two with short bowel syndrome and two from complications of corticosteroid treatment, a crude death rate of 33%. At that time conservative surgical management was recommended as they found that extensive resection was associated with increased death. Strictureplasty has therefore been used extensively in the last 10 years for the surgical treatment of short strictures in Crohn's disease. It is effective as recurrence rates are no higher than local resection,^{6,7} with the added advantage that strictureplasty conserves bowel and thus minimises the risk of developing the short small bowel syndrome.

Even though such patients pose considerable problems in medical and surgical management, there has been no analysis of the outcome in this group for more than 20 years. We have therefore analysed the outcome to determine appropriate medical and surgical management and their longterm prognosis. We have also analysed the outcome among patients with diffuse jejunoileitis to confirm or refute the suggestion that their disease becomes less aggressive with time. The clinical features and outcome have been compared with a group of patients with distal ileal Crohn's disease.⁸ The data from the second group have recently been updated.⁹

Patients and methods

PATIENTS

We reviewed the case records of all patients in whom a diagnosis of diffuse jejunoileitis has been established. Most patients were diagnosed as having diffuse jejunoileitis (29) at the time of their initial diagnosis, but five developed diffuse jejunoileitis later having initially had focal macroscopic disease elsewhere. We identified 37 such patients diagnosed between January 1960 and December 1991 from among a total series of 653 patients with Crohn's disease (5.7%). Three patients were excluded from the study because of incomplete case records, of whom one eventually died of small bowel cancer. Diffuse jejunoileitis was the main problem in all 34 patients, but in addition during the period of review 12 had colonic disease, nine involvement of the duodenum, and one oesophageal Crohn's disease. The mean age at diagnosis was 26.4 years (range 9-57) with a mean interval from onset of symptoms to diagnosis of 2.5 years (range 0-28). The diagnosis in women was made at a younger age (mean 23.5) compared with men (mean 31.6).

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The mean follow up was 16 years (range 7–30). Two patients have died during the period of review, the remainder are alive and under regular review.

DIAGNOSIS AND PRESENTATION OF DIFFUSE JEJUNOILEITIS

The diagnosis was based initially on typical radiological features, but was confirmed in nearly all patients both at laparotomy and histologically. All patients had typical clinical features and laboratory indices and care was taken to exclude other possible diagnoses including coeliac disease, tuberculosis, giardia, and other infections.

In some patients the initial symptoms were mild and referral for further investigation was only initiated when their symptoms became either more severe or persistent. This initially mild presentation in some patients accounted for the mean interval between the onset of symptoms and diagnosis of some 2.5 years.

Most patients presented with severe persistent abdominal symptoms that warranted early investigation and the diagnosis was usually readily established by the finding of abnormal laboratory results with anaemia, depressed serum albumin, and raised acute phase proteins, together with typical radiological appearances of the jejunum and ileum.

PRINCIPLES OF MANAGEMENT

The patients could usually be grouped (based on their clinical story and radiological appearances) into those with intermittent recurrent small bowel obstruction as a result of either single or multiple short strictures and those with systemic disturbance with diffuse inflammatory change without focal stricture formation. In both groups care was taken to correct anaemia, fluid and electrolyte depletion, and to identify those patients developing local septic complications. Alternative explanations for abdominal pain such as peptic ulcer, renal stones and gall stones, all of which occur more commonly in patients with Crohn's disease than the general population was also considered.

Laparotomy was usually recommended for patients with recurrent small bowel obstruction (more than 3–4 episodes). The diagnosis can then be confirmed macroscopically and histologically and the whole small bowel run over a balloon catheter to identify strictures visible on external inspection of the bowel and others elsewhere, which can look normal on the external surface. Strictureplasty was performed at all sites where the diameter of the bowel was <25 mm.

In those patients with inflammatory disease, 5-aminosalicylates were used initially, but most patients in this group were treated with oral corticosteroids, usually oral prednisolone in doses of 20–40 mg daily, depending on body weight, tapered over the course of a few months. For patients who relapsed when corticosteroids were reduced or withdrawn, azathioprine was added to the regimen, both as a steroid sparing agent and as an anti-inflammatory agent in its own right.

Patients were reviewed regularly in outpatients as often as once a week for patients with severe symptoms, but more commonly every 3 to 4 months. They were encouraged to attend in the interim should they develop new or recurrent symptoms. In this way it was possible to identify complications early and minimise the potential problems associated with malnutrition, weight loss, and severe sepsis. Outpatient and inpatient care has been managed in a Unit with close medical and surgical links including weekly meetings between physician, surgeon, radiologist, and histopathologist to consider appropriate management.

Results

CLINICAL FEATURES

Nearly all patients had clear cut abdominal symptoms, although in a few patients the symptoms were initially mild. The commonest presenting feature was colicky abdominal pain (91%) usually with other abdominal symptoms, including weight loss (62%) and diarrhoea (53%). There were isolated examples of uncommon presenting features including rectal bleeding from associated colonic disease, enterovaginal fistula, and growth retardation.

As expected, patients with Crohn's disease were more commonly smokers at the time of diagnosis, than the general population (53% *v* 26%).¹⁰ Only two of 34 patients (6%) had a family history of inflammatory bowel disease. During the period of review 11 patients (32%) suffered either depressive or anxiety symptoms sufficiently severe to warrant psychiatric referral and treatment.

MEDICAL MANAGEMENT

Twenty nine (85%) of patients were treated with corticosteroids (either ACTH or oral prednisolone). In 26 patients treatment was continued for at least six months and in 16 patients treatment was continued for more than one year. Among patients who had a partial or incomplete response to steroids, azathioprine was added in seven (21%) for its use as both a steroid sparing and as an anti-inflammatory agent.

Prolonged nutritional support was rarely required, probably because regular review and encouragement to attend immediately should symptoms recur or become more severe prevented serious weight loss. Thus only six patients received total parenteral nutrition, usually as a supportive measure for postoperative complications. Three patients received two or more courses. The modal duration of treatment was two weeks.

SURGICAL MANAGEMENT

An analysis of surgical management is mainly focused on diffuse jejunoileitis rather than for disease elsewhere. Twenty eight of 34 patients (82%) had at least one operation for diffuse jejunoileitis during review and if colonic surgery is included, all but one of the patients had at least one operation.

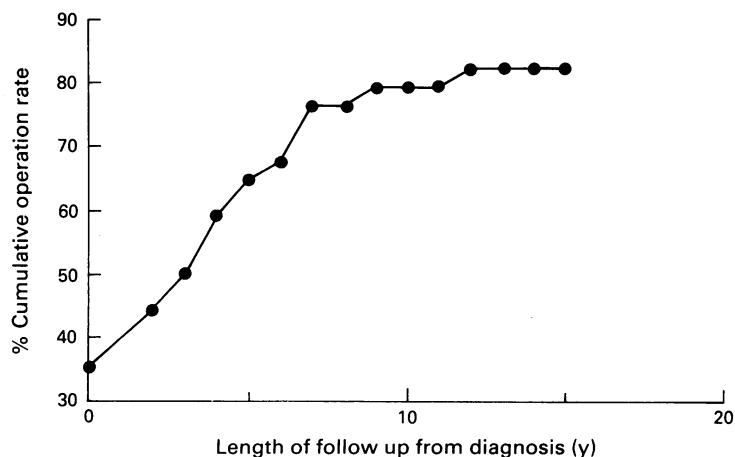
TABLE I Patients grouped according to the number of operative procedures

No of operations	No of patients
0	6
1	7
2	7
3	7
4	4
>4	3

In a total experience of 537 patient years the mean number of operations for diffuse jejunoileitis per patient year was 0.14 which is equivalent to one operation every 7.3 years. More than a third of the patients (n=12) had had surgery within the first 12 months after diagnosis and half the patients had been treated surgically by the third year of follow up (Table I, Fig 1). Patients having surgical treatment within the first 12 months after diagnosis had a higher than average operative rate subsequently (0.23 operations per year, equivalent to one operation every 4.4 years). During the period of review 21 (62%) had two or more operations.

It has been suggested that Crohn's disease may 'burn itself out' and become less aggressive with time. The data from this study suggest that this is the case for diffuse jejunoileitis. The proportion of patients who needed an operation was highest in the first 12 months after diagnosis (35%), and the annual operative rate was 15% thereafter. After 10 years the annual operative rate fell to 5.2% between years 11-15 and then to 2.6% in the years 16-20 (Fig 2). The number of patients followed up for more than 20 years was small, and precluded an accurate estimate of operative rates (Table II). Surgical intervention rates were higher in patients in whom the diagnosis was made at a young age with a negative correlation of 0.71 (p<0.001) (Fig 3). Duodenal involvement and diffuse jejunoileitis was associated with more frequent surgery. The operative rates in such patients were 0.3 per year, equivalent to one operation every 3.1 years.

The nature of the surgery for diffuse jejunoileitis has changed. Since 1981, strictureplasty has become the treatment of choice for patients with recurrent obstructive symptoms as a result of stricture formation. Resection is still the preferred treatment of choice for strictures more than 6 cm in length (Table III). Despite the



Year of follow up	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
No of patients having operation	12	3	0	2	2	2	1	3	0	1	0	0	1	0	0	0
Total patients under review	34	22	19	19	17	15	13	12	8	8	7	7	7	5	4	4

Figure 1: Cumulative operative rate with time in patients with diffuse jejunoileitis.

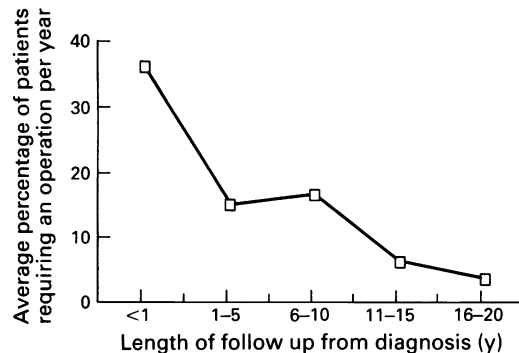


Figure 2: Average annual percentage of patients requiring an operation.

extensive disease and surgical challenges, there were only nine severe postoperative complications of abscess or fistula formation. Strictureplasty alone was associated with more complications (3/23) than resection alone (0/32). Bypass procedures were more commonly associated with postoperative complications (4/7), but this probably reflects a selection bias of the more severe problems where strictureplasty was inappropriate and resection proved difficult or impossible (Table IV).

Only two of the 34 patients have died (death rate 6%), one of perforation of the jejunum and the other of bronchogenic carcinoma. After a mean follow up of 16 years from diagnosis, 24 of 32 patients are currently well and symptom free and not receiving any specific medical treatment. Only eight have abdominal symptoms (including colicky abdominal pain, diarrhoea, or a high ileostomy output), of whom three are receiving corticosteroid treatment and one azathioprine. None of 32 patients are currently receiving nutritional support.

Discussion

Diffuse jejunoileitis is an uncommon manifestation of Crohn's disease and this is the largest reported series of patients thus far. The incidence of diffuse jejunoileitis as a manifestation of Crohn's disease has not changed since the review by Cooke and Swan,⁸ but as the Unit acts as a

TABLE II Diffuse jejunoileitis. Operative rates related to duration of follow up

Year of follow up	No of operations for diffuse jejunoileitis	Crohn's disease patient years	Average no of patients followed up in each quinquennium
0	12	34	34
1-5	24	170	34
6-10	24	153	31
11-15	8	113	23
16-20	4	64	13
21-25	3	30	6
26-30	0	7	1

TABLE III Changes in operative procedures for diffuse jejunoileitis with time

	Strictureplasty	Resection	Bypass
1961-1970	0	4	0
1971-1980	0	15 (75%)	5
1981-1990	37 (54%)	30 (44%)	2

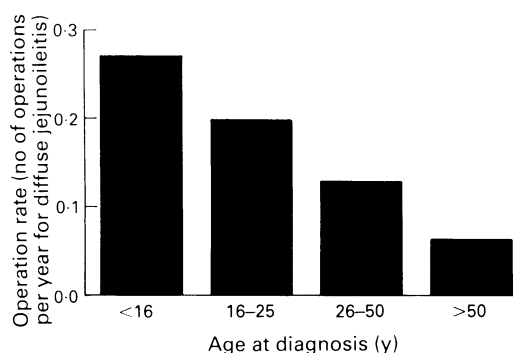


Figure 3: Age at diagnosis and operative rate for diffuse jejunoileitis.

referral centre for inflammatory bowel disease the true incidence in an unselected series is likely to be lower.

The incidence of diffuse jejunoileitis is higher among younger patients. The mean age at presentation was 26 years, compared with distal ileal disease of 33 years⁸ and colonic Crohn's disease (mean age 39 years).¹¹ This difference is likely to be accentuated if childhood onset Crohn's disease were included.

The main difficulty in diagnosis is that the initial symptoms in some patients may be mild, but within a short time most patients present with clear cut abdominal symptoms such as colicky abdominal pain, weight loss, and diarrhoea. Presentation with extraintestinal symptoms such as growth retardation does occur, but is rare in our experience.

Good quality radiological assessment of the small bowel can usually distinguish between single or multiple short fibrous strictures and more diffuse inflammatory change. We have usually accepted three to four episodes of severe obstructive symptoms as an indication for laparotomy in patients with stricture formation. At laparotomy, while some strictures are obvious on examination of the external surface of the gut, other significant strictures can only be identified by passing a balloon down the length of the gut. This has become a routine part of assessment at laparotomy to minimise the chance of missing significant strictures, particularly distal to sites of strictureplasty that may predispose to postoperative complications, such as enterocutaneous fistula formation.

Patients with persistent symptoms and no clear cut clinical or radiological evidence of fibrous stricture formation, are treated with oral prednisolone usually with good short term resolution of their symptoms. There is no clear drug trial evidence for the medium or longterm benefit for corticosteroids so we usually attempt to reduce

and withdraw steroids over a period of four to six months and if symptoms recur, add an immunosuppressive agent such as azathioprine. With time much of the inflammatory activity will resolve when re-assessed radiologically, but the healing phase is often accompanied by stricture formation and recurrent episodes of subacute intestinal obstruction, which if they persist or recur are an indication for laparotomy.

Surgical treatment has played an important part in the management of these patients. The average patient with diffuse jejunoileitis requires one operation every 7.3 years, which is twice the rate of surgical intervention in patients with distal ileal disease.⁸ Surgery is more commonly needed within the first 12 months after diagnosis in the younger patients and in those with associated duodenal involvement.

Strictureplasty, often multiple, has largely replaced resection and this approach has minimised the problems of the short small bowel syndrome and early recourse to surgical treatment has minimised the longterm use of corticosteroid treatment. Strictureplasty is associated with rather more complications than resection, but the complications usually respond to treatment.

It is encouraging for both the patients and their doctors that the disease becomes less aggressive with time and the incidence of surgical intervention falls with increasing length of follow up but even so the operative rates remain high in the first 10 years after diagnosis.

There were nine serious postoperative complications such as abscess or fistula formation among 74 operations (complication rate of 12%). Strictureplasty was associated with a rather higher complication rate than resection. Bypass procedures were associated with a particularly high complication rate, but this probably reflects severe disease that is not amenable to either strictureplasty or local resection. Bypass procedure has now largely been abandoned because of its association with malignant change.¹²

Total parenteral nutrition has played only a minor part in these patients and usually as postoperative support in the presence of complications. Elemental and enteral diets have received particular attention recently, but have not been used sufficiently frequently in this series to comment on their value.

Most patients have recurrent problems with high morbidity, which is reflected in the fact that nearly a third of patients have required psychiatric help for severe anxiety or depression, or a combination of the two and the liaison psychiatrist has played an important part in their management. Psychiatric symptoms were usually associated with active disease, for example, the most severely affected individual spent 257 days as an inpatient in the first five years from diagnosis.

Death rates have fallen. The use of strictureplasty has eliminated the deaths reported earlier from short small bowel syndrome and the conservative use of corticosteroids has eliminated the occasional steroid related death. There was only one disease related death in this series after perforation of the jejunum. The other patient died of an unrelated bronchogenic carcinoma.

TABLE IV Incidence of complications after operation

	No of operations	Complications	
		Abscess	Fistula
Resection	32	0	0
Strictureplasty	23	0	3
Resection and strictureplasty	12	0	2
Bypass	4	1	1
Bypass and strictureplasty	2	1	0
Bypass and resection	1	1	0

After a mean interval follow up of 16 years, 24 of 32 remaining patients are completely fit, well, and symptom free and only eight have abdominal symptoms, of whom three are receiving corticosteroids and one further patient is receiving azathioprine. Thus, diffuse jejunoileitis is a disease of high morbidity, particularly in the early years commonly requiring surgical intervention, but medium to longterm optimism is justified as most patients can now be restored to good health with minimal symptoms despite the high morbidity of the early years after diagnosis.

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