Ileal Crohn's disease is best treated by surgery

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Burrill Crohn *et al* in 1932 stated that "medical therapy is purely palliative and supportive . . . but in general the proper approach to complete cure is by surgical resection . . .".¹ However, by 1987 Bryan Brooke, a committed and creative inflammatory bowel disease surgeon, recognised that "the surgical stance is now one of reluctance . . . operation is withheld as a last resort when all else has failed to achieve palliation or support". Thus over half a century the surgical view radically changed from reckless enthusiasm to one of extreme conservatism. However, there has always been a fascination with the idea that early resection of localised ileal disease might result in long lasting remission and avoid unwanted complications that would inevitably lead to surgery.

There is no doubt whatsoever that surgery is indicated for an obstructing ileal stricture that fails to respond to medical or endoscopic therapy, for a right iliac fossa mass with internal or external fistulation, for uncontrolled bleeding, or when there is free perforation. However, in the absence of these complications there would seem to be no reason to recommend ileal resection. Early resection should therefore only be considered if it could be demonstrated that this intervention altered the natural history of the disease; as far as I am aware there is as yet no randomised clinical trial that has critically evaluated the possible benefits of early surgery versus medical therapy in uncomplicated localised ileal disease.

THE CASE AGAINST EARLY SURGERY

There is however compelling evidence that endoscopic, clinical, and surgical relapse rates after ileal resection are substantial. Endoscopic recurrence at one year is approximately 70% and at three years approaches 100%.^{2,3} At five years, 60% will have experienced a clinical recurrence and 25.6% and 11.9% of patients will require a second and third resection, respectively.⁴ There is also evidence to suggest that the length of recurrent disease is similar to the length of the involved segment before resection.⁵ Thus although one might argue that early resection for limited disease (<10 cm) has a low risk of creating a short bowel syndrome in later life, three resections of 60 cm could leave the patient with less than 100 cm of small intestine if the patient started life with a small intestinal length at the lower end of the normal range.⁶

THE CASE FOR MEDICAL THERAPY

On the more positive side, there is now clear evidence that effective medical therapy is available for (i) active ileal Crohn's disease, (ii) maintenance of remission, and possibly for (iii) prevention of postoperative recurrence.

Active ileal disease

Prednisolone is effective for the treatment of ileal Crohn's disease^{7,8} as is the rapidly metabolised new steroid budesonide, which has similar efficacy as oral prednisolone but with substantially less adrenal suppression.^{9,10} Controlled release mesalazine has also been shown to be effective in the treatment of active inflammation in patients with Crohn's disease¹¹ although Pentasa was only superior to placebo when given at a high dose of 4 g daily. The greatest decrease in Crohn's disease activity index occurred in patients with ileitis.¹² Budesonide has been found to be superior to Pentasa in controlling active Crohn's disease although unfortunately the comparison was made with a relatively low dose of Pentasa (2 g daily).¹³ Perhaps the most effective treatment for active, severe, recurrent ileitis would be azathioprine. D'Haens *et al* reported an uncontrolled series of 15 patients with severe Crohn's ileitis treated with azathioprine, six of whom had endoscopically demonstrated complete healing, five near complete, and three had partial healing.¹⁴

Maintenance of remission

There is clear evidence that azathioprine is effective in maintaining remission in patients with Crohn's disease¹⁵⁻¹⁸ and some evidence that budesonide 6 mg daily also reduces the probability of relapse in both ileal and ileocaecal Crohn's disease.¹⁹ The effect however appeared to diminish by the end of the one year follow up period. A role for methotrexate in the maintenance of remission in Crohn's disease is also well established.²⁰

Prevention of postoperative recurrence

The role of mesalazine in the prevention of postoperative recurrence has been highly controversial. Early randomised controlled studies found in favour of mesalazine²¹⁻²⁵; this observation was confirmed by a meta-analysis reported by Camma *et al* in 1997.²⁶ However, the large European Co-operative Crohn's Disease study by Lochs *et al* (2000)²⁷ was a largely negative study although there was a subgroup of patients with small intestinal disease who did benefit over an 18 month follow up period when treated with Pentasa 4 g daily. However, an update of the meta-analysis which included the study of Lochs *et al* failed to show a statistically significant result in favour of mesalazine.²⁸ It might be concluded therefore that although slow release 5-ASA may benefit a subgroup of patients following ileal resection, overall it would not appear to be a powerful agent in preventing postoperative recurrence in Crohn's disease.

An alternative agent to consider for the prevention of postoperative relapse is metronidazole. A small randomised controlled trial showed

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Debate

that metronidazole 20 mg/kg daily for three months significantly reduced endoscopic recurrence to 52% compared with 75% in the placebo group.²⁹ The effect was maintained at one year but significance was lost after two and three years of follow up. Metronidazole should be considered as a possible agent to prevent postoperative recurrence although further studies are required to confirm the benefit of longer term treatment, possibly using lower doses to avoid the well known adverse effects associated with long term use. The role of immunosuppressive drugs in the prevention of postoperative recurrence remains to be established.

Thus while medical therapy for ileal Crohn's disease cannot in any way be considered perfect, there is effective therapy for the treatment of active disease, maintenance of remission, and possibly even for reducing the risk of postoperative recurrence following ileal resection. Unfortunately, early ileal resection cannot offer any long term assurances and may in a small number of patients be associated with surgical complications including embarkation on a "slippery slope" towards short bowel syndrome. The emergence of new biotherapies such as the anti-tumour necrosis factor agents must mean that the wise physician should advise their patient to "hold on to the ileum" in the absence of absolute surgical indications for resection.

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