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Previous infliximab therapy and postoperative complications after proctocolectomy with ileum pouch anal anastomosis☆,☆☆,★

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Abstract

Background and aims: It is unclear whether infliximab treatment induces increased complication rates after surgery for ulcerative colitis. Aim was to compare complication rates after pouch surgery in refractory ulcerative colitis patients with versus without previous infliximab therapy.
Methods: We performed a retrospective study evaluating all patients who underwent an ileoanal J-pouch for refractory ulcerative colitis over a four-year period. Postoperative complications, infliximab use and time between last infliximab administration and restorative surgery were assessed. 1-stage procedures (proctocolectomy with pouch, with or without temporary diversion) and 2-stage procedures (emergency colectomy and subsequent completion proctectomy with pouch, with or without temporary diversion) were analyzed separately.
Results: Seventy-two patients were included; 33 underwent 1-stage procedure and 39 had 2-stage surgery. In the 1-stage group, 21 patients (64%) had previous infliximab therapy (median time between last infusion and surgery: 7.1 months (IQR 2.6-8.3)). Infliximab-treated patients had higher incidence of pelvic sepsis (5/21 vs. 0/12; risk difference 24%; 95% CI: 6 to 42, p=0.067) and non-infectious complications (8/21 vs. 1/12; risk difference 30%; 95% CI: 4 to 56, p=0.065). In the 2-stage group, 17 (44%) had previous infliximab therapy (median time between last infusion and surgery: 11.8 months (IQR 7.3-15.5)). Total, infectious, non-infectious

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complication rates and pelvic sepsis rates were similar for infliximab and non-infliximab patients in the 2-stage group.
Conclusions: This small study suggests that infliximab use prior to 1-stage restorative proctocolectomy in patients with UC is associated with increased incidence of pelvic sepsis. A 2-stage procedure in these patients should be considered.

1. Introduction

Steroid dependent ulcerative colitis (UC) can medically be treated with infliximab (IFX), a monoclonal antibody directed against the inflammatory cytokine TNF-alpha.[1] Since the approval of this drug in 2006, this therapy has often been applied as rescue therapy in order to prevent the need for surgery. When surgery is eventually indicated, it is not clear from the literature whether previous IFX treatment increases the risk of postoperative complications.[2–5]

UC that is refractory to all medical therapies should be treated surgically by means of a proctocolectomy with ileal pouch anal anastomosis (IPAA).[6] This procedure can be performed by a 1-stage procedure, being a proctocolectomy with IPAA, or a 2-stage procedure, in which an emergency colectomy is performed in the acute setting followed by a completion proctectomy with IPAA later on.[7] Both approaches can be performed with or without temporary ileal diversion.

Direct postoperative complications such as pelvic sepsis due to anastomotic leakage or a presacral abscess are known to increase the risk of pouch failure. This will significantly impair long-term quality of life.[8] It is therefore of utmost importance to minimize the incidence of pelvic sepsis after pouch surgery.

If IFX therapy that has been given within months before restorative surgery is associated with higher morbidity jeopardizing long-term pouch function, a 2-stage procedure can be chosen to increase the interval between IFX administration and restorative surgery. In that case, extending the period between last administration of IFX therapy and pouch surgery might lower the complication risk. Therefore, the aim of this study was to compare postoperative complication rates after restorative proctocolectomy with and without previous IFX therapy for medical refractory UC. For this purpose, 1- and 2 stage procedures were analyzed separately.

2. Materials and methods

For the purpose of this retrospective comparative study, patients requiring restorative proctocolectomy for medical refractory UC between January 1st 2006 and January 1st 2010 were retrieved from our institutional registries of all IPAA procedures. All patients were included, irrespective of the degree of colitis. Patients who underwent surgery because of dysplasia or malignancy were excluded.

Primary endpoints were the total complication rate within 30 days after surgery, the number of all infectious complications, the number of patients with pelvic sepsis and the number of non-infectious complications in patients with and without previous IFX therapy. Secondary endpoints were the direct postoperative hospital stay (PHS) and total postoperative hospital stay (THS), defined as PHS plus the additional hospitalization period if patients were readmitted within 30 days after surgery.

An infectious complication was defined as a complication leading to any kind of inflammation, including pelvic sepsis, surgical site infection, intra-abdominal abscesses and infectious complications other than abdominal. Pelvic sepsis was defined as anastomotic leakage, requiring reoperation and temporary ileostomy or presacral abscesses that could be treated percutaneously. Only clinically apparent pelvic sepsis was included. To detect pelvic sepsis, CRP measurements were routinely taken postoperatively and a CT scan was done at the slightest suspicion of leakage.

Non-infectious complications were all complications that did not meet the qualification of infectious complication. These included complications such as paralytic ileus, bleeding, dehydration, electrolyte disturbances, urinary retention or peroperative side damage.

All medical charts were reviewed. Patient characteristics were collected, as well as UC specific data. These disease specific characteristics included disease duration, extent of disease and preoperative medical therapy other than IFX. In case of previous IFX therapy, the time interval between last infusion and surgery and number of infusions were assessed. In patients who underwent a 2-stage procedure, time between acute colectomy and completion proctectomy with IPAA was determined.

In our hospital, a step-up treatment algorithm is applied for treatment of ulcerative colitis. Therefore, IFX was always applied as second line therapy in case of steroid refractory or dependent disease. In case surgery is needed, the preoperative condition was optimized by means of a short course of steroids, to lower levels of inflammation.

One-stage procedure and 2-stage procedures, both with or without temporary ileal diversion were analyzed separately. In the definitions we used, a procedure was defined a 1-stage procedure if proctocolectomy and creation of pouch were performed in one single operation, and also if a temporary ileostomy was created (this did not exclude patients from the 1-stage group). In all 2-stage procedure cases, an emergency resection was performed as the first stage, and a rest proctectomy with creation of pouch was done later as the second stage. Again, temporary ileostomies were performed in some, not excluding them from the 2-stage group.

A 2-stage procedure was performed in patients with an acute medical refractory exacerbation of UC requiring emergency colectomy. One-stage procedures were performed electively in patients with refractory disease without signs of acute disease activity. A temporary ileostomy was not routinely performed in all patients, but only in those considered to be at high risk of developing postoperative anastomotic leakage. Risk factors were considered steroids $>$20 mg/day, severe proctitis, difficult procedure or incomplete donuts.