Functional results and visceral perception after ileo neo-rectal anastomosis in patients: a pilot study

G I Andriesse, H G Gooszen, M E I Schipper, L M A Akkermans, T J M V van Vroonhoven, C J H M van Laarhoven

Abstract

Introduction—To reduce pouch related complications after restorative proctocolectomy, an alternative procedure was developed, the ileo neo-rectal anastomosis (INRA). This technique consists of rectal mucosa replacement by ileal mucosa and straight ileorectal anastomosis. Our study provides a detailed description of the functional results after INRA.

Patients and methods—Eleven patients underwent an INRA procedure with a temporary ileostomy. Anorectal function tests were performed two months prior to and six and 12 months after closure of the ileostomy and comprised: anal manometry, ultrasound examination, rectal balloon distension, and transmucosal electrical nerve stimulation (TENS). Function was subsequently related to the histopathology of rectal biopsy samples.

Results—Median stool frequency decreased from 15/24 hours (10–25) to 6/24 hours (4–11) at one year. All patients reported full continence. Anal sensibility, and resting and squeeze pressures did not change after INRA. Rectal compliance decreased (2.1 (0.7–2.8) v 1.5 (0.4–2.2) and 1.4 (0.8–3.7) ml/mm Hg (p=0.03)) but the maximum tolerated volume increased (70 (50–118) v 96 (39–176) (NS) and 122 (56–185) ml (p=0.03)). Decreasing rectal sensitivity was found: the maximum tolerated pressure increased (14 (8–24) v 22 (8–34) (NS) and 26 (14–40) (p=0.02)) and the rectal threshold for TENS displayed a similar tendency. All patients displayed a low grade chronic inflammatory infiltrate in neorectal biopsy samples before closure of the ileostomy, with no change during follow up.

Conclusions—The technique of INRA provides a safe alternative for restorative surgery. Stool frequency after INRA improves with time and seems to be related to decreasing sensitivity and not to histopathological changes in the neorectum. Furthermore, after the INRA procedure, all patients reported full continence.

(Gut 2001;48:683–689)

Keywords: restorative proctocolectomy; anorectal physiology; surgery; neorectum; intestinal mucosa transposition; recto-anal inhibition reflex

In patients with ulcerative colitis (UC) and familial adenomatous polyposis (FAP), the ileo-pouch anal anastomosis (IPAA) is the procedure of choice to restore continuity of the gastrointestinal tract after proctocolectomy. IPAA meets all the requirements for restorative surgery: the diseased tissue is removed, continuity of the digestive tract is restored, and a “neorectal” reservoir is created. However, many reports show a relatively high complication rate. Septic complications are especially common and are directly related to the formation of the ileo-anal anastomosis. Five to 10% of all IPAA patients eventually develop pouch failure. Although patient satisfaction after IPAA is high, “neorectal” function remains inferior to, for example, the ileorectal anastomosis: stool frequency of five versus three per day and imperfect continence in 30% versus 14% of all cases. In this respect, the ileorectal anastomosis would be the procedure of choice if all diseased tissue could be removed also.

In 1996 an alternative restorative procedure combining the virtues of ileoanal anastomosis and IPAA was developed in our department—the ileo neo-rectal anastomosis (INRA). The technique consists of rectal mucosa replacement by ileal mucosa. After successful experiments with INRA in pigs, a pilot study in patients was initiated. The initial clinical results of this study have been described recently. We now report in more detail on the results of gastrointestinal motility tests after INRA over a follow up period of one year.

Patients and methods

Between 1 January 1998 and 1 January 1999, nine patients with UC and two with FAP underwent an INRA procedure. Five patients were female, six patients were male, and median age was 36 years (range 20–53). All patients, except two with FAP (colon in situ) and one with UC (ileoanal anastomosis), had a diverting ileostomy after subtotal colectomy a median of six months (range 3–39) prior to the procedure.
INRA procedure. The patient selection procedure included a complete histopathological review of all biopsies and subtotal colectomy. Repeat rectal biopsies were performed after local treatment of proctitis. Only patients without transmural inflammation, inflammatory infiltrate, or fibrosis in the submucosa were selected for INRA. None of the patients had a history of faecal incontinence. Patients were asked about continence, deferral, and stool frequency during the day and at night, one, three, six, and 12 months after closure of the ileostomy.

Anorectal function tests were performed two months prior to and six and 12 months after the INRA procedure. Because it plays a major role in normal anorectal physiology, anorectal sensitivity was tested using transmucosal electrical nerve stimulation (TENS) and rectal distension. The reservoir function of the (neo)rectum was determined by rectal balloon distension. The quality of the anal sphincter complex was assessed by manometry and ultrasound examination. Patients were examined in the left lateral position, except for rectal balloon distension by barostat which was performed in the supine position.

Neorectal biopsy samples were obtained before and three, six, and 12 months after closure of the ileostomy. Histopathological examination of haematoxylin-eosin stained sections was performed to assess the quality of the mucous membrane and this was related to anorectal functioning. The ethics committee of the University Medical Centre Utrecht approved the protocol of the study. All patients gave written informed consent.

OPERATIVE TECHNIQUE

After subtotal colectomy, mucosectomy of about 15 cm of rectum was performed, from just above the peritoneal reflection to the dentate line. After removal of the complete rectal mucosal lining, a vascularised mucosa sling was created by removal of the seromuscular layer of the distal 15–20 cm of the terminal ileum (fig 1A). Analogous to the formation of a split skin graft, multiple longitudinal incisions of 5–10 mm were made in the mucosa to adapt the sling to the diameter of the rectum and to enable slough to be evacuated from between the rectal cuff and mucosal sling. An incision of approximately 5 cm was made laterally in the denuded rectal wall to facilitate entrance of the mucosal vascular pedicle. Next, the mucosal sling was introduced into the denuded rectum and sutured to the dentate line (fig 1B). Finally, an ileorectal anastomosis was made and a temporary diverting ileostomy was constructed. A gynaecological pack was introduced into the neorectum to fix the mucosal sling to the rectal muscular wall and to absorb blood and debris. The pack was left in situ for 48 hours. Up to one week after removal of the gynaecological pack, the neorectum was rinsed daily with normal saline. The diverting ileostomy was closed three months after the INRA procedure.

TRANSMUCOSAL ELECTRICAL NERVE STIMULATION (TENS)

TENS is a simple and accurate method for the reproducible quantitative assessment of anal and rectal sensitivity. During TENS the afferent sensory fibres innervating the anal
Ileo neo-rectal anastomosis

The operative procedure was technically successful in all patients. In the first days after the INRA procedure, four patients developed fever and somatic pelvic floor muscle dysfunctions. Seventy percent of the patients developed anorectal dysfunctions. Rectal symptoms were common and included urgency, incontinence and tenesmus. One patient complained of an anal fistula. One patient complained of an anal fistula. One patient complained of an anal fistula. One patient complained of an anal fistula. One patient complained of an anal fistula. One patient complained of an anal fistula.

**ENDO ULTRASONOGRAPHY**

Anal and rectal ultrasonography was performed before operation and six months after INRA to determine structural changes in the sphincter (scar tissue, defects or fragmentation of the internal or external sphincter) and to assess the transmural architecture of the neorectum. With a 10 MHz rotating ultrasound probe (B and K Medical, Denmark) an overview was made of the ileal wall, neorectum, and anal sphincter complex. The thickness of the internal anal sphincter (IAS) was measured at the point of maximum thickness. The results were compared with normal values, as reported by Bartram and Frudinger using the same technique, and patients also served as their own controls.

**RECTAL SENSITIVITY TO DISTENSION**

(Neo) rectal pressure sensitivity was examined by means of balloon distension using an electronic barostat (Distender II; G&J Electronics Inc., Ontario, Canada). This is a computer controlled injection-aspiration air pump, enabling isobaric distensions with high reproducibility. The balloon consisted of a cylindrical polyethylene bag with infinite compliance up to a maximum volume of 1000 ml (10 cm length) connected to the barostat by an 18 Ch polyvinyl tube (Mallinckrodt Medical, Athlone, Ireland). After introducing the bag, it was unfolded by temporary insufflation of 150 ml of air. Subsequently, the minimal distension pressure (MDP) was found by increasing intrabag pressure up to the point at which respiratory excursions were clearly visible. Rectal distensions were performed in two minute steps in a single staircase protocol with 2 mm Hg pressure increments above MDP. During each distension step the bag volume was measured and recorded by the computer enabling subsequent data analysis. In the last 30 seconds of each step the patient was asked about the first sensation of rectal distension (FS), first desire to defecate (FD), or maximum tolerable pressure (MTP). FS, FD, and MTP are the pressures (mm Hg) at which the sensation was first noticed by the patient. The barostat bag was deflated immediately after reaching MTP.

**STATISTICAL ANALYSIS**

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 7.5). Continuous data were tested using the two tailed Wilcoxon signed rank test. Nominal data were tested using the chi² test. Follow up of stool frequency was tested by the Friedman test. Alpha was set at 0.05.

**Results**

INRA RELATED COMPLICATIONS AND STOOL FREQUENCY

The operative procedure was technically successful in all patients. In the first days after the INRA procedure, four patients developed fever.
and rectal pain. Retention of pus in the neorectum was discovered by physical examination and successfully treated by rinsing the neorectum with normal saline. In six cases mild stenosis of the anal anastomosis developed and was successfully treated by digital dilatation. No other INRA related complications were recorded during follow up.

At one, three, six, and 12 months after closure of the ileostomy, both total and nocturnal stool frequency had decreased significantly (fig 2). After 12 months of follow up, nine patients were receiving medication to control stool frequency and consistency. Three patients experienced occasional soiling at night (one/week), resulting in occasional (<1/month) nocturnal incontinence for liquid stools in one patient. No patient was dependent on continence pads and all patients were able to defer defecation for more than one hour.

TENS

Figure 3 displays the results of anal and rectal TENS before and six and 12 months after closure of the ileostomy. There was no difference in median threshold for anal TENS preoperatively compared with after INRA: 6.0 (4–14) v 6.0 (3–9) mA, respectively (p>0.05). The median threshold for rectal sensation increased after INRA from 26 mA (16–75) preoperatively to 36 mA (13–99) and 46 mA (24–70) at six and 12 months, respectively (p>0.05).

ANAL SPHINCTER PRESSURES, RECTAL COMPLIANCE, AND MAXIMUM TOLERATED VOLUME

Table 1 displays median ASL, MARP, MASP, FR, and FRI. Both MARP and MASP were above or within the normal range in all patients, both before and after INRA. Median FR was similar at all three times. However, FRI improved postoperatively, reaching statistical significance after 12 months. One patient with occasional nightly faecal incontinence had the lowest MARP and a low FRI of 4.1 minutes. RAIR was present in nine patients preoperatively but only one patient tested positive three months after INRA and another one
Table 1 Anal sphincter manometry indices, (neo) rectal compliance, and MTV before and after ileo neo-rectal anastomosis (INRA) (median (ranges))

<table>
<thead>
<tr>
<th></th>
<th>Preoperatively</th>
<th>6 months</th>
<th>12 months</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL (cm)</td>
<td>3 (1.4–4.1)</td>
<td>2.5 (1.8–3.7)</td>
<td>2.5 (1.8–3.8)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MARP (mm Hg)</td>
<td>61 (46–99)</td>
<td>53 (38–84)</td>
<td>57 (47–76)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MASP (mm Hg)</td>
<td>152 (53–266)</td>
<td>141 (30–304)</td>
<td>148 (61–266)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>FR (mm Hg/min)</td>
<td>−32 (11–160)</td>
<td>−28 (7–94)</td>
<td>−22 (7–54)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MDP</td>
<td>4.3 (0.5–8.9)</td>
<td>5.1 (12.0–11.6)</td>
<td>5.5 (3.6–9.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Compliance (ml/mm Hg)</td>
<td>2.1 (0.7–2.8)</td>
<td>1.5 (0.4–2.2)</td>
<td>1.4 (0.8–3.7)</td>
<td>0.03</td>
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<tr>
<td>MTV (ml)</td>
<td>70 (50–118)</td>
<td>96 (39–176)</td>
<td>122 (56–185)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Significant differences between 12 month results for FRI and MTV, and compliance at six months, compared with preoperative levels. The normal range for FRI is −42 (SD 43) mm Hg/min and for FRI 3.3 (4.3) minutes. ASL, anal sphincter length; MARP, maximal anal resting pressure; MASP, maximum anal squeeze pressure; FR, fatigue rate; FRI, fatigue rate index; MTV, maximum tolerated volume.

Table 2 Results of rectal sensitivity testing by barostat balloon distension. First sensation (FS) and first desire (FD) are the pressures at which the patient first noticed rectal distension and desire to defecate, respectively.

<table>
<thead>
<tr>
<th>Median pressure above MDP (mm Hg)</th>
<th>Preoperatively</th>
<th>6 months</th>
<th>12 months</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDP</td>
<td>14 (12–20)</td>
<td>16 (12–20)</td>
<td>16 (12–16)</td>
<td>&gt;0.05</td>
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<tr>
<td>Sensory thresholds</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>FS</td>
<td>4 (2–6)</td>
<td>5 (0–24)</td>
<td>10 (2–22)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>FD</td>
<td>10 (8–18)</td>
<td>12 (8–34)</td>
<td>18 (10–34)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MTP</td>
<td>14 (8–24)</td>
<td>22 (8–34)</td>
<td>26 (14–40)</td>
<td>0.03</td>
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</tbody>
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*MDP, minimal distension pressure; MTV, maximum tolerated volume.

Discussion

The main object of INRA is to avoid complications related to the restorative procedure in the pelvis. With only mild stenosis as a “reservoir related” complication, this goal has been achieved. The next two major objects are to preserve anal sphincter function and to create a compliant reservoir to ensure full continence, the ability to defer defecation, and an acceptable stool frequency.

ENDOULTRASONOGRAPHY

The ultrasonographic image demonstrated no structural damage to the anal sphincter complex either before or after INRA. All patients displayed well defined circularity of the IAS and external anal sphincter, without defects or fragmentation. Furthermore, the median maximum thickness of the IAS was unchanged after surgery: 1.8 (1.4–4.1) mm before versus 1.9 (1.0–3.9) mm (p>0.05) after INRA and was within the normal range. All of the different layers of the rectal wall were identifiable and no structural changes were evident.

RECTAL SENSITIVITY TO DISTENSION

The median thresholds for FS, FD, and MTP increased after INRA at six months and reached statistical significance after 12 months for FD and MTP (table 2). During rectal distension no contractions were recorded.

HISTOPATHOLOGICAL EXAMINATION OF BIOPSY SAMPLES

Before closure of the ileostomy, all patients, including two with FAP, displayed a flattened mucosa with shortening of the villi but normal covering of goblet cells and enterocytes. The lamina propria showed an overall low grade mainly chronic inflammatory infiltrate, with only sporadic activity and crypt destruction. Furthermore, the number of eosinophils in the mucous membrane had increased.

Biopsy samples taken at follow up displayed the same low grade lymphoplasmacellular infiltrate in the lamina propria and level of crypt destruction as before restoration of gastrointestinal continuity. Furthermore, the length of the villi, quality of the brush border, and number of goblet cells and enterocytes remained unchanged.

In three patients, at three, four, and 12 months of follow up, the postoperative period was complicated by severe “neoproctitis” with symptoms of increasing stool frequency, cramps, and change in consistency to more liquid stools. Biopsy samples showed destruction of the mucous membrane with subtotal villous atrophy, ulceration, a dense mixed inflammatory infiltrate in the lamina propria, and multiple crypt abscesses, resembling changes found during pouchitis. In all three patients neoproctitis was successfully treated with antibiotics and steroids, resulting in disappearance of the mixed inflammatory infiltrate and recovery of the INRA mucosa.

year after INRA (χ², p=0.0003). Although median rectal compliance decreased significantly after INRA (p=0.03), it did not improve during follow up. However, MTV improved during follow up, reaching statistical significance at 12 months (table 1).

Although Holdsworth and Johnston reported different threshold electrosensitivity for the anal canal before and after mucosectomy, results of TENS in this study indicate that sensitivity did not change after mucosectomy, suggesting that pudendal nerve endings were not damaged. Furthermore, results of TENS were supported by the fact that all patients were able to discriminate between flatus and faeces, a function ascribed to sensitivity of the anal mucosa. Impaired internal sphincter function after mucosectomy is believed to be the result of both damage to the autonomic nervous system and damage to smooth muscle. Although in this study anal mucosectomy was performed, manometry showed equal MARP and ASL, before and after INRA. Furthermore, we found no gaps or tapering of the IAS during ultrasonographic examination, or a decrease in IAS thickness, indicating that INRA had not resulted in damage to the smooth muscle of the IAS. The fact that only superficial stitches are used to align the mucosal suture to the dentate line instead of a full thickness anastomosis to the anus could explain why no damage was found to the IAS. External sphincter function was also unaffected after INRA. In addition, FRI increased above preoperative values. An explanation could be that most patients had a defunctioning stoma before INRA, causing a deteriorated condition of the striated musculature by “lack of training”. Consequently, the increasing FRI indicates postoperative recovery.
The second main object of the INRA procedure is creation of a plant reservoir and preservation of sensory function, ensuring effective control of defecation.28 Although neorectal compliance after INRA is reduced compared with preoperative levels, MTV increased significantly during the 12 month follow up period.40 Reduced neorectal compliance after INRA in a preliminary experimental animal study could be explained by the presence of a thin fibrous band in the submucosa,29 as was diagnosed by ultrasonography and histopathological examination. However, in this study ultrasonography did not reveal a fibrous band in any of the layers of the neorectal wall and since no resection specimen is available it remains unclear what caused the reduction in neorectal compliance in patients.

Moreover, stool frequency improved significantly during follow up. Mean defecation frequency in this pilot study, however, was higher than reported after IPAA (4–8 times per day and about once during the night) in expert series. The question is why patients with low neorectal compliance and MTV after INRA displayed a stool frequency in approximately the same range as IPAA patients. In contrast with patients with IPAA, but similar to the normal rectum, INRA patients did not show neorectal large pressure waves induced by rectal distension. After IPAA, the threshold volume for these large pressure waves is more a determinant of stool frequency and urgency than MTV.47–49 Therefore, the actual functional volume is much smaller. Because INRA patients do not display large pressure waves, the functional volume is larger and more closely related to MTV. Furthermore, rectal sensitivity testing revealed increasing thresholds for PD and MTP; implying decreasing sensitivity of the neorectum with time.50 Thresholds for rectal electrosensitivity showed a similar trend after INRA. Therefore, knowing that compliance during follow up did not improve, increasing stool frequency after INRA seems to be related more to decreasing rectal sensitivity than improving MTV. This could explain why INRA patients did not experience the urge to defecate and retained the capacity to defer defecation. Furthermore, improved stool frequency cannot be explained by the results of histopathology because the inflammatory infiltrate was of low activity and did not change during follow up. Only in three cases of transient “neoproctitis” could the presence of a dense mixed inflammatory infiltrate, ulceration, and severe destruction of the mucous membrane account for the high stool frequency. Analogous to patients with active UC, frequent and urgent defecation during neoproctitis is probably caused by hypersensitivity of the neorectum induced by severe inflammation.27 31 This rectal hypersensitivity is thought to be caused by sensitisation of rectal nerves afferents.32 33 On the other hand, sensitisation of rectal afferents is not found in UC patients with quiescent colitis.27 30 Therefore, it is not likely that the low grade inflammatory infiltrate found in INRA patients affects anorectal functioning. Whether decreasing sensitivity of the neorectum is a result of progressive “desensitisation” of rectal afferent fibres after a longer lasting hypersensitivity induced by the INRA procedure is not clear.

Finally, fine tuning of anorectal function in healthy subjects is demonstrated by RAIR. Although the IAS is also innervated by sympathetic nerves via the hypogastric (presacral) nerves, RAIR is believed to be mainly dependent on the enteric nervous system.34 Although preservation of anal sensitivity and internal sphincter pressure seem to indicate that the autonomic nervous system was not affected by mucosectomy, RAIR was absent in all but one patient after INRA. The exact pathways for RAIR are still unknown, but it may be hypothesised that as the myenteric plexus between the rectal muscle layers is left intact, RAIR is most dependent on the submucosal plexus which presumably is destroyed during mucosectomy. However, after IPAA without mucosectomy the reflex remains intact despite the fact that the rectum is dissected,35 lacking both the submucosal and myenteric plexus of the rectal wall. Therefore, it seems likely that RAIR does not originate from the rectal wall but from the upper anal canal and that its pathways are destroyed during anal mucosectomy. Reappearance of RAIR after INRA could indicate regrowth of intramural nerves to the sphincter complex.56 The same effect is found in patients after IPAA.57 However, all INRA patients retained the ability to discriminate flatus from faeces despite absence of RAIR. As the ability to discriminate between gas, liquid, and solid is ascribed to relaxation of the IAS by RAIR,49 allowing the rectal contents to come into contact with the anal mucosa, we postulate that the presence of the RAIR is less important than effective sensation in the anal canal.

Conclusions

Stool frequency immediately after INRA is considerable. However, after 12 months all patients had a functional outcome comparable with IPAA patients. The improvement in stool frequency after INRA seems to be related to decreasing sensitivity and not to normalisation of histopathology of the neorectum. Despite the fact that total anorectal mucosectomy is performed during the INRA procedure, no damage was found to anal sphincter function, resulting in full continence. The technique is more complex than the IPAA procedure; the learning curve for the experienced colorectal surgeon is rather steep. Time will tell whether the investment in adopting this technique will pay off in better outcome in terms of function and quality of life compared with the IPAA procedure. This pilot study has shown that the INRA technique provides a safe and more preserving type of restorative surgery for patients with UC and FAP.

GI Andriesse is a Janssen-Cilag research fellow.

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Gut 2001 48: 683-689
doi: 10.1136/gut.48.5.683

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