

The ileo neo-rectal anastomosis in patients with familial adenomatous polyposis: a prospective case series with long-term follow up

S. de Zeeuw*, J. T. Heikens*, H. G. Gooszen† and C. J. H. M. van Laarhoven*

*Departments of Surgery and †Operating Rooms/Research Unit, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Received 15 February 2011; accepted 7 June 2011; Accepted Article online 3 September 2011

Abstract

Aim In patients with familial adenomatous polyposis (FAP), removal of the colonic mucosa is essential to reduce the lifetime risk of developing cancer. For this purpose, ileo-pouch anal anastomosis (IPAA) has been the gold standard, but morbidity related to the dissection of the pelvis remains substantial. In an attempt to reduce the procedure-related complications of pelvic dissection, ileo-neo-rectal anastomosis (INRA) has been developed. In this case series of FAP patients, the long-term functional results, morbidity and quality of life (QoL) of the INRA procedure were evaluated and compared with its early outcome.

Method Long-term follow up of a consecutive group of eight FAP patients with an INRA procedure (between 1998 and 2005) was undertaken. Data on functional results, complications, manometry and endoscopy were recorded prospectively.

Results Eight patients with FAP underwent the INRA procedure. The median number of defaecations over 24 h

was five. No pelvic sepsis or bladder dysfunction occurred. One patient, in whom concomitant Crohn's disease was diagnosed in retrospect, was converted to IPAA. In the INRA patients, no sexual dysfunction occurred. Endoscopic examination showed normal mucosa without any evidence of polyp formation.

Conclusion Restorative surgery by means of the INRA procedure yields good functional results in FAP patients, without any pelvic dissection-related morbidity or regrowth of polyps in the neo-rectum.

Keywords FAP, INRA, restorative surgery

What is new in this paper?

The long-term results of the INRA procedure, as an alternative to standard surgical procedures for FAP patients, are described.

Introduction

After colectomy for familial adenomatous polyposis (FAP), several surgical options are possible: the construction of an ileo-rectal anastomosis (IRA) leaving the rectum *in situ*, total proctectomy with an ileostomy or construction of an ileo-pouch anal anastomosis (IPAA).

The functional results of IRA are superior to those of an IPAA, but lifetime surveillance of the rectum for polyps is necessary and the cumulative risk of cancer is 11% after 15 years follow up [1]. In a select group of patients, restorative surgery, such as IPAA, is an option and is dependent on age, phenotype and presence and

number of rectal adenomas. In an attempt to reduce the procedure-related complications of pelvic dissection during IPAA, ileoneo-rectal anastomosis (INRA) has been developed [2,3]. Using INRA a pelvic dissection is avoided, the colonic and rectal mucosal linings are removed and oro-anal continuity is restored by constructing an ileal mucosal transposition into the rectum (Fig. 1).

The medium-term results (2 years follow up) of this case series were presented in 2005 [4]. The aim of the current study was to evaluate the long-term results of INRA for FAP in terms of function, morbidity and quality of life (QoL). These data are needed to decide on further implementation of this technique. Functional results at this stage were comparable to those reported in the literature for IPAA [5].

Correspondence to: S. de Zeeuw, Department of Surgery, Radboud University Nijmegen Medical Centre, PO box 9101, 6500 HB Nijmegen, The Netherlands. E-mail: s.dezeeuw@chir.umcn.nl

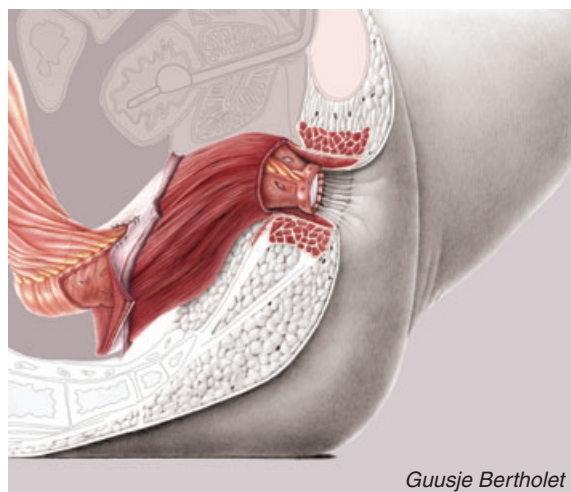


Figure 1 Sagittal plane of male pelvis with terminal ileum sling transposition in the rectal sleeve.

Method

Epidemiological data, preoperative endoscopic findings, operative details, postoperative complications and length of hospital stay, clinical outcome and bowel function were recorded prospectively for a series of patients who underwent INRA for FAP from 1998 to 2005. The ethics committee of the University Medical Centre Utrecht and of the St Elisabeth Hospital Tilburg approved the study protocol. All patients gave written informed consent. The INRA was performed as described by Van Laarhoven [3,6] (Fig. 1). All procedures were carried out by two surgeons who had extensive experience in restorative surgery. Patient follow up with data registration was as described previously. All results were compared with the results of the 2-year follow up [6].

Functional results

Functional result was assessed in terms of frequency of defaecation and faecal (in)continence. The degree of faecal incontinence was assessed using the Vaizey score [7]. A score of 0–5 represents normal continence, 6–10 minor incontinence, 11–15 moderate incontinence and 16–24 severe incontinence.

Ano-rectal physiology and endoscopy

Anal manometry was carried out as described previously [6]. Endoscopic assessment with biopsies at four levels was performed to evaluate adenomatous mucosa and dysplasia microscopically. Endoscopy and anal manome-

try were carried out preoperatively, at 6 and 12 months after surgery and then annually.

Quality of life measurements

The definitions of QoL as established by the World Health Organization Quality of Life Group (WHOQOL group) were used [8]. A set of questionnaires was completed preoperatively and 6 and 12 months after operation and then annually. The questionnaire package contained a socio-demographic questionnaire (education level, marital status, children and income) and the Dutch version of the World Health Organization Quality of Life assessment instrument (WHOQOL-100), the development of which was based on definitions of QoL as mentioned before [9]. For general health status (HS) measurements the RAND-36, Dutch version, was included [10–12]. Reference scores were derived from the manuals of the WHOQOL-100 and are based on a healthy Dutch population [13–15]. An independent researcher analysed all questionnaires to avoid any form of bias.

Statistical analysis

Descriptive statistics were used to summarize patient demographics, clinical data and complications. Anal manometry results were analysed with a paired samples test. QoL and HS results were analysed with the *t*-test. Results are expressed as median and ranges. Significance was defined as $P < 0.05$. All analyses were performed with the Statistical Package for Social Sciences (SPSS® version 16.0, Chicago, Illinois, USA).

Results

A consecutive group of eight FAP-INRA patients, operated on between 1998 and 2005, were included. Patient characteristics are summarized in Table 1. Median follow up was 7 years (range 4–12 years).

One patient had her INRA converted to a pouch because of repeated stenosis and inflammation. For the

Table 1 Baseline characteristics of FAP patients with INRA.

	FAP with INRA ($n = 8$)
Sex ratio (M:F)	5:3
Mean age at restorative procedure (years)	29.3
Subtotal colectomy and INRA in one procedure (n)	7

same reason, her pouch was excised ultimately and she received a permanent ileostomy. Revision of the neo-rectal excision specimen and the proctocolectomy specimen by two independent pathologists demonstrated that this patient not only suffered from FAP, but also showed signs of Crohn's disease.

Clinical data

Median operation time was 375 min (25th and 75th quartiles 338 and 489 min). Median blood loss was 1100 ml (25th and 75th quartiles 500 and 2500 ml). There was no postoperative mortality. All temporary diverting ileostomies were closed after 3 months.

Functional results

Median number of defaecations per 24 h at 7 years follow up was 5 (25th and 75th quartiles 5.0 and 5.5). Median number of nocturnal bowel movements was 0.5 (25th and 75th quartiles 0.5 and 1.0). The median Vaizey incontinence score was 1 (25th and 75th quartiles 0 and 6.0).

Morbidity

No pelvic sepsis or bladder dysfunction occurred. None of the patients reported sexual dysfunction. None of the remaining seven patients developed a stenosis.

Late complications occurred in three patients: a small bowel obstruction requiring adhesiolysis, a peri-anal abscess after 8 years, which required drainage, and an ileostomy-related hematoma, which required surgical drainage. No one episode of pouchitis was observed. Altogether, 13 complications occurred in eight patients.

Ano-rectal physiology

Follow-up ano-rectal physiology was investigated in seven patients. Median follow up was 6 years (range 4–12). The

median anal resting pressure, maximum anal squeeze pressure and compliance increased nonsignificantly compared with 2 years follow up, while the maximum tolerated volume remained stable (Table 2).

Endoscopy

Follow-up endoscopy was performed in seven patients. Median time to endoscopy was 7 years (range 1–12). In all patients a healthy neo-rectal reservoir and noninflamed mucosa was seen. No signs of formation of adenomatous polyps were seen. In one asymptomatic patient, ulcerations were present. Routine biopsies at four levels showed no signs of dysplasia.

Quality of life

Health status and the separate domains of the WHO-QOL-100 were scored preoperatively and at 2 and 7 years follow up. Whereas preoperative values showed a decreased spirituality dimension (HS) and physical and emotional role limitations (WHOQOL-100), the data after 2 and 7 years showed no significant differences to the reference scores, except for an improved perception of general health at 7 years follow up. The results are displayed in Tables 3 and 4.

Discussion

This study has evaluated whether the 7-year long-term results of INRA are consistent with the 2-year results and assesses the long-term risk of polyp recurrence in the neo-rectum.

INRA showed good functional results, which remained consistent over time, without reservoir-related complications in seven patients. Good ano-rectal physiological measurements reflect a good functional outcome.

The main advantage of the INRA concept is that it combines total removal of diseased colorectal mucosa,

Table 2 Anoreservoir manometry FAP patients with INRA.

<i>n</i> = 7	Before operation	2 years follow up	6 years follow up	Normal values
Resting pressure (mmHg)	75.0 (38–105)	53.0 (34–68) <i>P</i> = 0.3	61.0 (38–68) <i>P</i> = 0.5	37.5–75
Squeeze pressure (mmHg)	150.0 (90–248)	149 (60–240) <i>P</i> = 0.8	178.5 (67–263) <i>P</i> = 0.5	150–180
Maximum tolerated volume (ml)	167.0 (97–295)	167 (127–239) <i>P</i> = 0.5	160.0 (79–300) <i>P</i> = 0.8	200
Compliance (ml/kPa)	35.0 (22–60)	31 (13–127) <i>P</i> = 0.8	24.0 (12–32) <i>P</i> = 0.4	35–80

Median values, ranges in parentheses. Statistical analysis (*P* values) of 2-year results compared with preoperative values and of 7-year results compared with 2-year results.

Table 3 Health status.

Domain	Ref score	Pre-op	2 years	7 years
Overall QoL	15.6	15.7	13.7	15.3
Physical health	14.6	12.7	12.7	15.0
Psychological health	14.7	13.9	13.2	15.0
Level of independence	16.3	14.2	14.3	16.7
Social relationships	15.1	16.6	16.2	14.9
Environment	15.8	19.1*	16.4	15.7
Spirituality	13.3	9.0*	13.7	12.3

The scores on the seven domains of health status before operation, and after 2 and 7 years of follow up compared with the reference score in a normal population. * $P < 0.05$.

Table 4 WHOQOL-100.

Dimension	Ref score	Pre-op	2 years	7 years
Physical functioning	79.9	89.8	83.3	97.5
Social functioning	86.1	62.5	75.0	100.0
Role limitations, physical	78.9	33.3*	58.3	100.0
Role limitations, emotional	83.6	44.4*	33.3	66.7
General mental health	76.6	58.7	56.0	84.0
Energy/fatigue	67.5	45.0	48.3	75.0
Bodily pain	80.5	87.3	75.0	100.0
General health perception	71.6	72.0	69.0	92.0*

The scores on the eight dimensions of the WHOQOL-100 before operation and after 2 and 7 years of follow up compared with the reference score in a normal population. * $P < 0.05$.

thus avoiding the risk of developing rectal cancer (which is a known complication after IRA), and avoids pelvic dissection, which carries a high risk of pelvic sepsis and autonomic nerve damage (such as observed after IPAA).

In contrast to the INRA procedure for UC, in which the rectal mucosa dissection remains laborious, the INRA procedure for FAP is technically straightforward and easy to perform. Operation time was longer and blood loss was higher compared with the open IPAA procedure [16]. However, the INRA procedure combines subtotal colectomy with the restorative part of the treatment in one procedure. Seven years follow up, including repeated endoscopy and biopsies, did not reveal residual or recurrent growth of rectal mucosa or adenomatous polyps, establishing the INRA procedure as a valuable and safe alternative to ileorectal anastomosis for a select group of patients.

There exists a chance of dysplasia in the pouch after IPAA. A recent study shows evidence for mucosal detoxification in the pouch, and thus the possibility of pouch metaplasia [17]. It is possible that a similar process could occur in the ileal mucosa after INRA. More research is needed in this area.

Pelvic dissection-related complications did not occur in INRA patients and this contrasts with data that show an almost 4% sexual dysfunction and 10% pelvic sepsis rate after IPAA [18].

The present study has its limitations. The small number of patients precludes definite conclusions. However, the follow up in the patients is 7 years and the functional results and low complication rate remain stable.

INRA is not the only alternative restorative procedure. Nowadays, the pouch operation can also be performed by a rectal dissection close to the bowel wall ('close-rectal dissection') instead of a mesorectal excision [19]. Close-rectal dissection has advantages in ulcerative colitis, because the rectal mucosa dissection (with the INRA procedure) can be very laborious in an inflammatory bowel. In FAP patients it has to be demonstrated whether close-rectal dissection is more advantageous than an INRA procedure. In addition, mucosectomy and a stapled IPAA is another alternative, which combines the advantage of the total removal of rectal mucosa and the advantage of better functional results [20]. More research is needed to put these three techniques into perspective.

In conclusion, in this pilot study with long-term follow up, the INRA technique has fulfilled the criteria of a good

alternative to the IPAA or IRA for FAP patients. Based on these results, INRA seems to be a safe, valuable and straightforward restorative procedure for FAP patients in whom complications of a pelvic dissection should be avoided. Long-term studies with a larger population are needed to confirm this preliminary conclusion.

References

- 1 Sinha A, Tekkis PP, Rashid S *et al*. Risk factors for secondary proctectomy in patients with familial adenomatous polyposis. *Br J Surg* 2010; **97**: 1710–5.
- 2 Peck DA. Rectal mucosal replacement. *Ann Surg* 1980; **191**: 294–303.
- 3 van Laarhoven CJ, Andriess GI, Back WA *et al*. The ileo neorectal anastomosis: an experimental study on development of the surgical technique and theoretical background. *Colorectal Dis* 2001; **3**: 82–94.
- 4 Strijbos SA, Huetting WE, Schipper ME *et al*. The ileo neo rectal anastomosis (INRA) in patients with familial adenomatous polyposis: clinical results at two years. *Colorectal Dis* 2005; **7**: 354–9.
- 5 Tekkis PP, Lovegrove RE, Tilney HS *et al*. Long-term failure and function after restorative proctocolectomy – a multi-centre study of patients from the UK National Ileal Pouch Registry. *Colorectal Dis* 2010; **12**: 433–41.
- 6 van Laarhoven CJ, Huetting WE, Schipper ME *et al*. Ileo-neorectal anastomosis: medium- and long-term follow-up of 37 patients. *Dig Surg* 2004; **21**: 371–8.
- 7 Vaizey CJ, Carapeti E, Cahill JA *et al*. Prospective comparison of faecal incontinence grading systems. *Gut* 1999; **44**: 77–80.
- 8 The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med* 1995; **41**: 1403–9.
- 9 De Vries J, Van heck GL (1995) *De Nederlandse versie van de WHOQOL-100 [The Dutch version of the WHOQOL-100]*. Tilburg University.
- 10 Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. *Health Econ* 1993; **2**: 217–27.
- 11 McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993; **31**: 247–63.
- 12 Bowling A. Health care research: measuring health status. *Nurs Pract* 1991; **4**: 2–8.
- 13 The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. *Soc Sci Med* 1998; **46**: 1569–85.
- 14 Masthoff ED, Trompenaars FJ, Van Heck GL *et al*. Validation of the WHO Quality of Life assessment instrument (WHOQOL-100) in a population of Dutch adult psychiatric outpatients. *Eur Psychiatry* 2005; **20**: 465–73.
- 15 VanderZee KI, Sanderman R, Heyink J. A comparison of two multidimensional measures of health status: the Nottingham Health Profile and the RAND 36-Item Health Survey 1.0. *Qual Life Res* 1996; **5**: 165–74.
- 16 Ahmed AU, Keus F, Heikens JT *et al*. Open versus laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous polyposis. *Cochrane Database Syst Rev* 2009; CD006267.
- 17 Friederich P, Berkhout M, Roelofs HM *et al*. Decreased levels of mucosal detoxification enzymes in the pouch of patients with familial adenomatous polyposis. *Br J Surg* 2006; **93**: 1108–14.
- 18 Huetting WE, Buskens E, van der Tweel I *et al*. Results and complications after ileal pouch anal anastomosis: a meta-analysis of 43 observational studies comprising 9,317 patients. *Dig Surg* 2005; **22**: 69–79.
- 19 Rink AD, Radinski I, Vestweber KH. Does mesorectal preservation protect the ileoanal anastomosis after restorative proctocolectomy? *J Gastrointest Surg* 2009; **13**: 120–8.
- 20 Bulow S. Mucosectomy and stapled pouch-anal anastomosis in familial adenomatous polyposis. *Colorectal Dis* 2012; **14**: 68–70.