

Full Length Research Paper

Surgical management of familial adenomatous polyposis in pediatric patients through ileoneorectal anastomosis

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Van Laarhoven et al. proposed restorative proctocolectomy with ileoneorectal anastomosis (INRA) to treat familial adenomatous polyposis (FAP). Although it is considered a reproducible surgical technique with low complication rates, there have been few reports of its use in the literature, with no reports addressing pediatric patients. Our pediatric surgery group has been using this technique since 2005. The aim of this study was to analyze the clinical and functional results obtained from the use of this technique to treat children with FAP. Clinical data were retrieved from the children's medical records. The patients were interviewed regarding their medical conditions, and they received a physical examination to assess their clinical condition, defecation patterns and aspects related to quality of life. Eight patients with a diagnosis of FAP underwent surgical treatment with INRA. The average age was 12.25 (\pm 2.9) years. The median operative time was 465 minutes, and times ranged from 240 minutes to 600 minutes. There were no intraoperative complications. Three patients required reoperation (2 by flanges and 1 by twisting of the protective ileostomy). The median follow-up time was 36 months (5–120 months). Most patients (57%) presented with regular bowel movements, soft stools and a stool frequency of up to 5 times per day. Two patients had soiling (1 case with daily losses and 1 case with weekly losses). Total proctocolectomy with INRA proved to be a safe and effective technique for the treatment of children with FAP, and it offered satisfactory clinical results.

Keywords: familial adenomatous polyposis; children; surgery; restorative proctocolectomy; ileoneorectal anastomosis.

List of Abbreviation

FAP, Familial adenomatous polyposis; IRA, total colectomy with ileum rectum anastomosis; IPAA, restorative proctocolectomy with an ileo pouch anal anastomosis; INRA, restorative proctocolectomy with ileoneorectal anastomosis.

INTRODUCTION

Familial adenomatous polyposis (FAP) is a rare genetic

syndrome, clinically expressed by the presence of hundreds to thousands of adenomatous polyps in the colon. FAP has an estimated incidence of 1:10,000 live births (Lelli Jr, 2012). It originated from mutations in the

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APC gene and is transmitted vertically with familial occurrence as an autosomal dominant condition of complete penetrance. Furthermore, up to 30% of cases originate from spontaneous mutations (Hyer, 2012).

The colonic polyps usually appear at 10 years of age, with greater intensity after puberty. The adenoma-carcinoma sequence is the expected evolution in all untreated cases (Lelli Jr, 2012). Thus, the current recommendations suggest initiating the investigation by sigmoidoscopy or colonoscopy in individuals with a family history of FAP from 10 years of age (Alkhoury et al., 2010; Levin, 2008). The presence of numerous adenomatous polyps, typically more than one hundred, characterizes the disease. A biopsy of at least ten of these polyps should be sufficient to confirm the diagnosis (Lelli Jr, 2012). A positive genetic test, gastrointestinal symptoms (such as abdominal pain and defecation bleeding) and the presence of high-grade dysplasia are some of the criteria that anticipate the diagnostic investigation and surgical treatment of pediatric patients (Alkhoury et al., 2010; Lelli Jr, 2012; Levin, 2008).

Surgery is the only recognized treatment to reduce the risk of colorectal cancer in patients with FAP (Alkhoury et al., 2010). The basis of this treatment is the surgical removal of the entire colon and rectal mucosa. The greatest challenge faced by surgeons is to develop a technique that allows this removal and, at the same time, provides an appropriate quality of life. These aspects are even more relevant when the surgery is performed in pediatric patients, as their results may lead to lifetime sequelae. There are several surgical techniques described, each with strengths and weaknesses, and the most common methods currently are total colectomy with ileum rectum anastomosis (IRA) and restorative proctocolectomy with an ileo pouch anal anastomosis (IPAA) (Lelly Jr, 2012; Gorgun and Remzi, 2004; Seetharamaiah et al., 2009).

Van Laarhoven et al. (1999) proposed the use of restorative proctocolectomy with ileoneorectal anastomosis (INRA), which allowed the manufacture of a physiological fecal reservoir. Despite this advantage, and the fact that this technique had been proved to be highly reproducible with low complication rates, there have been few reports of INRA in the literature. The published articles that have provided a description of this surgical technique, which have all been written by the same authors, described adult patients with only one pediatric patient at 15 years old (Andriessse et al., 2001; deZeeuw et al., 2012 a; Heikens et al., 2013 a,b,c; O'Riordan et al., 2012; Stijbos et al., 2005; Van Laarhoven et al. 1999; Van Laarhoven et al. 2001; Van Laarhoven et al. 2004). Thus, the aim of this study was to analyze the clinical and functional results obtained after performing restorative proctocolectomy with INRA in children with FAP.

METHODS

An observational, ambispective cohort study was conducted in patients under 18 years of age who underwent restorative proctocolectomy with INRA for the treatment of FAP from 2005 to 2014 at the Botucatu Medical School Hospital and Bauru State Hospital. All cases were operated by the same surgical team following the technical principles described by Van Laarhoven et al. (2004). After subtotal colectomy, the rectal muscle wall is denuded by mucosectomy and a transposition of 15–20 centimeters of healthy terminal ileal mucosa is placed in the rectal sleeve and anastomosed to the nonsquamous epithelium just above the dentate line. A temporary diverting ileostomy is closed some months postoperatively (Van Laarhoven et al., 2001; Van Laarhoven et al., 2004).

The medical records of 8 patients were retrospectively analyzed to obtain clinical and demographic data. Subsequently, the patients were requested to participate in a medical interview in which they completed a standardized questionnaire to evaluate the current clinical conditions, focusing on the defecation patterns and aspects related to quality of life. All patients and/or their caregivers gave their written informed consent, and the Research Ethics Committee of the Botucatu Medical School approved the project.

The following information was obtained from medical records:

- Preop: age at diagnosis, family history of FAP, clinical symptoms, results of endoscopy and histopathological tests performed.

- Intraop: age at surgery, surgical time, need for blood transfusion and complications.

- Postop: early and late complications, hospital stay, time elapsed until the closure of the diverting ileostomy, need for new surgical approaches, histopathological diagnosis of the surgical specimen and results of endoscopy and biopsies performed during the postoperative follow-up.

In the medical interview, data related to functional outcomes (e.g., number of daily bowel movements, fecal incontinence, and characteristics of the stools), quality of life (e.g., activity restrictions and the need to use diapers), and the presence of postoperative sequelae (e.g., urinary incontinence, abdominal pain and sexual dysfunction) were collected. Questionnaire to evaluate the functional outcome (Figure 1), the Vaizey Score for Evaluation of Fecal Incontinence and the Bristol Scale for Analysis of Stool Consistency, were applied (de Zeeuw et al., 2012 b; Heaton et al., 1999; Martinez et al., 2012; Vaizey et al., 1999).

Figure 1. Questionnaire applied to evaluate the functional outcome

1. How many times a day do you evacuate? _____
2. Do you lose stool in your underwear without warning? Yes No
If yes, how many times per day? ____
3. Are the surgery consequences disrupting your life in some way? Yes No
4. Do you need to wear diapers? Yes No
5. Do you use any medication to regulate bowel movements? Yes No
If yes, which one(s)? _____
6. Do you need a special diet? Yes No
If yes, which one(s) _____
7. Do you feel abdominal pain? Yes No
If yes, how often? _____
8. After surgery, have you ever had to return to the hospital for abdominal symptoms (abdominal pain, vomiting, cessation of the elimination of flatus and feces)?
 Yes No If yes, how many times? _____
9. Have you ever had perianal rashes? Yes No
10. If yes, did you treat it? Yes No
If yes, which treatment(s) _____
11. Do you lose urine in the underwear without warning? Yes No
If yes, how many times per day? _____
12. Do you have a sexual life? Yes No
If yes, have you ever had any sexually related problems? Yes No
13. Do you use any medication regularly? Yes No
If yes, which one(s)? _____
14. Are there any other health problems that have required medical attention?
 Yes No If yes, which one(s)? _____

RESULTS

Between 2005 and 2015, eight patients under 18 years of age underwent restorative proctocolectomy with INRA for the surgical treatment of FAP. One patient (the most recent case) was in the fifth post-operative month and still had a protective ileostomy. For this case only, we used the clinical data and information from the perioperative period and did not request a medical interview to obtain information on functional outcomes and late follow-up.

All patients had a family history of FAP. Four patients (50% of cases) had clinical complaints of abdominal pain and/or hematochezia at diagnosis, which were the earliest indication of diagnostic research and surgical treatment. The diagnosis of FAP was confirmed by colonoscopy with the histopathological examination of polyps endoscopically resected, which revealed the presence of tubular adenomas with low-grade atypia in

four cases and high-grade atypia in the other four patients (Table 1). There were neither complications during the intraoperative period nor the need for conversion to another surgical technique (Table 2).

In all cases, the histopathological examination of surgical specimens confirmed the diagnosis of FAP, revealing the presence of multiple polyps with low-grade atypia and a proximal surgical margin free from polyps. The median follow-up time was 36 months, with a minimum of 5 months (the most recent case) and a maximum of 120 months. The median time to the ileostomy closure was 8 months, with a minimum of 4 and maximum of 10 months.

Most of the patients (57%) presented with regular bowel habits with soft stools and stool frequency of up to 5 times daily. Only two patients had soiling (patient number 5 showed daily losses and patient number 6 presented with weekly losses). The median value of the

Table 1. Patients' clinical data at diagnosis

| | |
|--|-------------|
| Gender (male: female) | 3:5 |
| Mean age and standard deviation (years) | 12.25 ± 2.9 |
| BMI mean and standard deviation (kg/m ²) | 18.5 ± 4.9 |
| Patients presenting symptoms at diagnosis (%) | 4/8 (50%) |

Table 2. Summary of Perioperative data

| | |
|---|---------------|
| Median (minimum and maximum) of surgical time (minutes) | 465 (240–600) |
| Percentage of patients requiring blood transfusion | 25% |
| Median (minimum and maximum) length of stay in the ICU (days) | 2 (1–3) |
| Median (minimum and maximum) of hospital stay (days) | 10 (8–20) |

Table 3. Functional results of the medical interview

| Patient number | Follow-up (months) | Number of evacuations per day | Vaizey Score | Classification based on Vaizey score | Bristol Scale | Need for Diapers | Use of constipating medication | Perianal dermatitis |
|----------------|--------------------|-------------------------------|--------------|--------------------------------------|---------------|------------------|--------------------------------|---------------------|
| 1 | 120 | 5 | 1 | Normal | 6 | No | No | No |
| 2 | 96 | 5 | 2 | Normal | 6 | No | No | No |
| 3 | 60 | 7 | 0 | Normal | 6 | No | No | No |
| 4 | 36 | 3 | 3 | Normal | 6 | No | No | No |
| 5 | 24 | 2 | 12 | Moderate incontinence | 5 | No | No | No |
| 6 | 12 | 8 | 7 | Low incontinence | 6 | No | No | No |
| 7 | 5 | 9 | 2 | Normal | 6 | No | No | No |

Vaizey scores was 2 (minimum 0 and maximum 12). The data relating to functional results in medical interviews during the postoperative period are summarized in Table 3.

No deaths occurred during the follow-up period. Similarly, there were no cases of inflammation of the neorectum or pelvic sepsis. With respect to early complications, two patients had partial dehiscence of INRA, receiving conservative treatment, and three patients developed anastomotic stricture and were submitted to anal dilatation with success. Two patients required early reoperation. One presented with kinking of the ileostomy and received surgery on the 7th post-operative day, and the other presented with flanges and received surgery on the 10th post-operative day. Regarding late complications, there were no reports of urinary incontinence or sexual dysfunction in patients with an active sex life. One patient had bowel obstruction 24 months after the ileostomy closure and received surgical treatment for lysis of adhesions.

The follow-up endoscopy period varied from 1 to 7 years and was performed in six patients. In all examinations, neorectum reservoirs were identified without inflammatory mucosal signs. Routine biopsies in

4 levels of the neorectum showed no signs of dysplasia in the ileal mucosa.

DISCUSSION

Surgery is the only recognized treatment to reduce colorectal cancer risk in patients with FAP (Alkhoury et al., 2010). The goals are complete removal of the colorectal mucosa in addition to an adequate quality of life, with fecal continence and an acceptable bowel movement frequency. Several surgical techniques may be used; however, none of them fully achieve these goals (Lelly Jr, 2012; Gorgun and Remzi, 2004; Seetharamaiah et al., 2009).

A total proctocolectomy with permanent ileostomy prevents colorectal cancer. However, maintaining a permanent ostomy has physiological and psychological consequences. In addition, extensive pelvic dissection can result in sexual impotence and urinary incontinence. For these reasons, this is not a surgical technique of choice in the pediatric population and is therefore restricted to adult patients with low rectal cancer associated with FAP or sphincter dysfunction (Lelly Jr, 2012; Campos and Alves, 2012).

Another surgical technique commonly used in the treatment of FAP is total colectomy with IRA that aims to preserve the rectum as a reservoir organ that is essential for fecal continence. It results in less surgical morbidity and few complications. Furthermore, results show adequate stool frequency (3 to 4 times daily on average) and fecal continence in most patients (Strijbos et al., 2005). This method, however, does not guarantee removal of the mucosa of the rectum, and therefore, the incidence of postoperative colorectal cancer rates could reach 25% after 15 years (Iwama and Mishima, 1994). The choice of this technique requires permanent follow-up of the rectum with endoscopic examinations at intervals of four to six months, with the resection and cauterization of adenomas. The need for further surgery for rectal excision occurs in up to 40% of patients over the entire life span (Vasen et al., 1996).

A restorative proctocolectomy with an IPAA is currently the surgical technique of choice in the treatment of FAP. Originally described by Parks and Nicholls (1978), the procedure consists of a total proctocolectomy with preservation of the anal sphincter and construction of a reservoir from an ileal tube that is sutured to the anal canal. This technique fulfills three fundamental attributes: removal of the diseased tissue, maintenance of the continuity of the digestive tract and creation of a neo-reservoir (Campos and Alvez, 2012; Parks and Nicholls (1978). Thus, eradication of all colorectal mucosa prevents adenoma-carcinoma evolution, and the ileal reservoir ensures, in most cases, an acceptable stool frequency. However, it is a markedly complex surgical procedure with high rates of post-operative morbidity, reaching up to a 10% failure rate. The main complications are related to the ileal pouch, such as "pouchitis," pelvic sepsis, fecal incontinence, stenosis of the ileo-anal anastomosis, perianal and vaginal fistulas and intestinal obstruction (Gorgun and Remzi, 2005; Heikens et al., 2012; Lovegrove et al., 2007; Seetharamaiah et al., 2009; Stavlo et al., 2003; Strijbos et al., 2005; de Zeeuw et al., 2012).

Thus, in an attempt to reduce complications related to the ileal pouch, van Laarhoven et al. (1999) proposed restorative proctocolectomy with INRA. The great advantage of this method is the combination of the strengths of the two previous techniques. While the procedure totally removes the rectal mucosa, reducing the risk of cancer, prevents pelvic manipulation and retains a markedly physiological fecal reservoir (Andriessse et al., 2001; deZeeuw et al., 2012 a; Heikens et al., 2013 a,b,c; O'Riordan et al., 2012; Stijbos et al., 2005; Van Laarhoven et al., 1999; Van Laarhoven et al., 2001; Van Laarhoven et al., 2004).

In our study there were no specific INRA-related complications or the need to perform a surgical conversion to another technique. Despite technical difficulties, the necessary reoperations were only required

for complications that were not directly related to the restorative procedure. INRA would not be expected to change the percentage of intestinal obstructions, a complication related to laparotomy. Two patients required flanges lysis and one patient required a review of the diverting ileostomy. Other complications (partial dehiscence and stenosis of the anastomosis) were treated clinically with satisfactory results.

The functional results were considered to be quite satisfactory. Only two patients had soiling and were in bowel management. No patient required the use of diapers or constipating medications. Moreover, there were no reports of urinary incontinence or sexual dysfunction.

The current study has its limitations related to the limited sample size. On the other hand, the indications for surgical treatment for FAP in children are very restricted in patients in their childhood (Alkhoury et al. 2010; Lelly Jr, 2012; Levin et al., 2008). In addition, there are only two studies reporting INRA exclusively for FAP in adults, with the maximum of 8 patients (Strijbos et al., 2005; deZeeuw et al., 2012a). Our study is the first to present the results of INRA in children with FAP and we observed that the restorative proctocolectomy with INRA proved to be a safe and effective technique, with appropriate clinical and functional outcomes for the treatment of children with FAP. Long-term follow-up studies using this technique are necessary to confirm these preliminary results.

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