Functional outcome and quality of life after rectal resection
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Chapter 8

THE CUMULATIVE RISK
OF DEVELOPING POLYPS OR MALIGNANCY
AT THE ILEAL POUCH-ANAL ANASTOMOSIS IN PATIENTS
WITH FAMILIAL ADENOMATOUS POLYPOSIS

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Abstract

Background/Aims: Restorative proctocolectomy (RPC) with an ileal pouch-anal anastomosis (IPAA) is performed in an increasing number of patients with FAP. Two techniques are currently used to construct an IPAA, i.e., a double stapled (DS) anastomosis between pouch and anal canal and mucosectomy and handsewn (HS) ileoanal anastomosis at the dentate line. Although this procedure is thought to abolish the risk of colorectal adenoma, an increasing number of case reports have been published on adenoma development at the anastomotic site. To evaluate the overall cumulative risk of developing adenomatous polyps after IPAA and to compare the cumulative risk after either anastomotic technique.

Methods: 126 consecutive FAP patients undergoing a RPC were identified from polyposis registries in The Netherlands, Denmark, Italy, Germany and New York.

Results: Life table analysis was used to calculate the cumulative risk for developing polyps in ninety-seven patients with at least one year of endoscopic follow-up (median 66, range 12 - 188 months). A double stapled anastomosis was used in thirty-five patients, whereas in sixty-two patients a hand-sewn anastomosis with a mucosectomy was performed. In 13 patients, polyps developed at the anastomotic site, four with severe and four with moderate dysplasia. None developed a carcinoma. The cumulative risk for developing a polyp at the anastomotic site was 8% (95% C.I. 2 - 14%) at 3.5 years and 18% (95% C.I. 8 - 28%) at 7 years, respectively. The risk for developing a polyp at the anastomotic site within 7 years was 31% for patients with a double stapled versus 10% for patients with a hand-sewn anastomosis with mucosectomy (p = 0.03 (log-rank test)).

Conclusion: Since FAP patients undergoing a RPC with either a double stapled or a hand-sewn anastomosis have a substantial risk for developing adenomatous polyps at the anastomotic site, lifelong endoscopic surveillance is mandatory in both groups.
Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominantly inherited disease caused by mutations in the APC-gene on chromosome 5. The disease is characterized by hundreds of adenomatous polyps throughout the colon and rectum. Most patients develop polyps during the second and third decade of life. Without timely surgical intervention, virtually all patients will develop colorectal cancer, often by the fourth decade.¹

Until recently, the most frequently used procedure for FAP patients was a colectomy and ileo-rectal anastomosis (IRA).² This is a technically simple procedure to perform, with a low complication rate and good functional outcome.³ However, there are some disadvantages to this procedure, since the cumulative risk of cancer evolving in the rectal stump is reported to be 15 % after 25 years of follow-up,⁴⁻⁷ and more than 40 % of patients with an IRA will need a secondary proctocolectomy after 20 years because of uncontrollable polyps.⁷ The alternative to an IRA in FAP patients is a proctocolectomy with an ileal pouch-anal anastomosis (IPAA). This procedure provides removal of virtually all the rectal mucosa thereby reducing the risk for recurrence of adenomatous polyps or adenocarcinoma. The IPAA can be constructed with either hand sutures or a stapling device. The hand sewn (HS) anastomosis is in general preceded by a mucosectomy down to the dentate line to eliminate all mucosa at risk. The double stapling (DS) technique can potentially leave rectal mucosa behind but reduces operating time and is reported to have better functional results.⁸

Although an IPAA is thought to abolish the risk of colorectal adenoma development, an increasing number of case reports have been published on adenomatous polyps or carcinoma developing at or distal to the IPAA.⁹⁻¹³ These findings raise concern about the at-risk mucosa left behind at the anastomotic site. The present study was therefore undertaken in order to evaluate the risk of developing adenomas or cancer at the anastomosis after IPAA. In addition, the risk was compared between patients with a double-stapled anastomosis and those with a hand-sewn anastomosis with a mucosectomy. The possible impact of a coexistent colorectal carcinoma at the time of the proctocolectomy, on the recurrence of polyps, was also assessed.
CHAPTER 8

Patients and methods

Six centers or registries where IPAA procedures for FAP are regularly performed and registered, agreed to participate in the study; Academic Medical Center Amsterdam, Academic Hospital Rotterdam, Academic Hospital Nijmegen, Leiden University Medical Center, Memorial Sloan-Kettering Cancer Center, New York and the Italian and Danish polyposis registries. At each center or registry, all FAP patients who had undergone an IPAA procedure were selected. A questionnaire was mailed to all participants requesting information on: date of IPAA, presence of synchronous cancer at the time of surgery, type of anastomotic procedure, post operative complications, type of follow-up of the patients (endoscopic or digital examination), polyps (location, grade of dysplasia) or cancer, interval between IPAA and diagnosis of adenomas, treatment, need for pouch excision and the date of last follow-up.

Statistical analysis:
Proportions of events were compared by means of chi-square tests with p values < 0.05 considered statistically significant. Cumulative incidence of polyps was analyzed by Kaplan-Meier survival analysis and differences between the two different anastomotic techniques compared by log-rank test. All reported p values are two-tailed. Cox regression analysis was used to quantify the effect of the presence of synchronous cancer at the time of surgery and the two different anastomotic techniques on the recurrence of polyps. Possible confounding effects of presence of synchronous cancer at the time of surgery and the two anastomotic techniques on recurrence of adenomas at the anastomotic site was studied using a Cox proportional hazard model.

Results

Between 1981 and 1997, 126 consecutive FAP patients underwent a restorative proctocolectomy with IPAA at six different centers or registries. In 97 patients, follow-up was performed by endoscopy for at least one year (median 66, range 12-188 months), 29 patients were screened by means of rectal digital examination or were surveyed for less than one year. In the endoscopically surveyed group, there were 41 women and 56 men with a median age of 35 years (range, 16-60 years) and a median age at the time of surgery of 30 years (range, 10-55 years). Out of the 97 endoscopically surveyed patients, 62 had a hand-sewn (HS) anastomosis with mucosectomy and 35 patients had a double-stapled anastomosis (DS). The number of control endoscopies per year differed between
the different study participants. The median number was one endoscopy per year, ranging from three times per year to once per two years.

In five patients a pouch excision followed by a permanent ileostomy construction was performed. One permanent ileostomy was made in a patient because of recurrent distal obstruction due to an irresectable desmoid tumor. Two patients had a permanent ileostomy constructed because of anastomotic pouch complications. In one patient the pouch had to be excised due to recurrent cancer and in one patient the pouch was removed due to unmanageable polyp formation in the pouch. The median interval between restorative proctocolectomy and pouch excision was 17 months (range, 2 - 131 months). The date of pouch excision was taken as date of last follow-up in these five patients.

With a median follow-up of 78 months (range, 25 - 137 months) 13 out of the 97 endoscopically surveyed patients developed adenomatous polyps at the anastomotic site. The interval between IPAA and diagnosis and the histological stage of the adenomas are outlined in Table 1.

Table 1: Adenomatous polyps present in 13 of 97 FAP patients at the ileal pouch-anal anastomosis

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Interval * (months)</th>
<th>Histology</th>
<th>type of anastomosis</th>
<th>Pouch excised (reason)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>female</td>
<td>41</td>
<td>moderate dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>male</td>
<td>23</td>
<td>severe dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>41</td>
<td>male</td>
<td>40</td>
<td>moderate dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>female</td>
<td>55</td>
<td>severe dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>female</td>
<td>25</td>
<td>moderate dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>male</td>
<td>52</td>
<td>mild dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>female</td>
<td>43</td>
<td>mild dysplasia</td>
<td>DS</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>male</td>
<td>74</td>
<td>severe dysplasia</td>
<td>HS</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>49</td>
<td>female</td>
<td>81</td>
<td>mild dysplasia</td>
<td>HS</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>47</td>
<td>male</td>
<td>95</td>
<td>mild dysplasia</td>
<td>HS</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>56</td>
<td>male</td>
<td>131</td>
<td>moderate dysplasia</td>
<td>HS</td>
<td>pouch dysfunction</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>female</td>
<td>24</td>
<td>severe dysplasia</td>
<td>HS</td>
<td>multiple polyps in the pouch</td>
</tr>
<tr>
<td>13</td>
<td>22</td>
<td>male</td>
<td>15</td>
<td>mild dysplasia</td>
<td>HS</td>
<td>-</td>
</tr>
</tbody>
</table>

* Time from IPAA procedure to development of adenomatous polyps. HS = hand sewn anastomosis; DS = double stapled anastomosis.

The cumulative risk for developing an adenoma at the anastomotic site was 8% (95% C.I. 2-14%) at 3.5 years and 18% (95% C.I. 8-28%) at 7 years, respectively (Figure 1).
Six out of 13 patients who developed polyps at the anastomotic site had a HS anastomosis and a mucosectomy whereas the other seven patients had a DS anastomosis. The risk for developing adenomatous polyps at the anastomotic site within 7 years was 10% for patients with a hand-sewn anastomosis and mucosectomy. This is significantly less than the risk for patients with a double stapled anastomosis which is 31% (p = 0.03 (log-rank test)). (Figure 2). The relative risk to develop polyps at the DS anastomotic site was 1.9 times (95% C.I. 1.2 - 3.2)) that of patients with a HS anastomosis and a mucosectomy. (p < 0.01 (Univariate Cox regression))

A coexisting colorectal carcinoma at the time of surgery was present in 20 patients, 11 of them had a HS anastomosis with a mucosectomy and 9 had a DS anastomosis. The relative risk for developing polyps at the anastomotic site in case of a synchronous colorectal carcinoma was not increased (RR = 1.2 (95% C.I. 0.7 - 2.1)). The inclusion of the variable, ‘presence of synchronous cancer at the time of surgery’ did not change the relative risk for the two different anastomotic techniques in a substantial way.
Discussion

Restorative proctocolectomy with an IPAA has as compared to conventional colectomy and ileo-rectal anastomosis, the advantage that theoretically all rectal mucosa at risk is eliminated. The functional results of this procedure are improving as morbidity and pouch failure incidence are reported to decrease. The incidence of sexual and bladder dysfunction is very low. Finally quality of life is rated by IPAA patients to be satisfying or very satisfying although this has been assessed by non validated questionnaires. These advantages might explain that IPAA is performed in an increasing number of FAP patients.

Recent studies show that restorative proctocolectomy with an IPAA does not seem to provide a total risk reduction as illustrated by case reports on adenomatous polyps and cancer arising at the anastomosis after IPAA. There are some reports indicating that histologically examined anorectal mucosal strippings, taken at the time of the proctocolectomy, contained dysplasia from 85.7% to even up to 100%. Two other studies showed the presence of polyps or

Figure 2: Hazard curves for the cumulative incidence of polyp recurrence at the anastomotic site in FAP patients who underwent a proctocolectomy with a hand sewn ileal pouch-anal procedure and mucosectomy (dotted line) and for FAP patients who underwent a proctocolectomy with a double stapled ileal pouch-anal procedure (continuous line) (log rank: p = 0.03). Censored case are presented by +, number of patients at risk are presented below.
dysplasia in surgical doughnuts or biopsies taken just distal to the pouch-anal anastomosis in patients who underwent a restorative proctocolectomy for FAP.\textsuperscript{10,23} Investigators of the Mayo Clinic reported that small islets of residual rectal mucosa were found buried in the fibrous tissue between the rectal muscular cuff and the ileal serosa in four out of 26 ileo-anal specimens excised on average 17 months after construction of the ileo-anal anastomosis.\textsuperscript{24} Moreover, Hoehner \textit{et al.}\textsuperscript{12} described an adenocarcinoma arising at a straight ileo-anal anastomosis in a 34-year-old woman, 20 years after proctocolectomy. Pathologic review of the posterior excenteration specimen revealed an invasive adenocarcinoma arising at the junction of the dentate line. Von Herbay \textit{et al.}\textsuperscript{13} described an adenocarcinoma, arising at the anastomotic site in a 33-year-old woman, 8 years after her HS pouch procedure with a mucosectomy. Histopathology of the excised anal canal showed some islets of residual rectal-type mucosa, situated between the ileal pouch and the anal transitional zone with a moderately differentiated adenocarcinoma infiltrating into the internal anal sphincter. Despite this information, the absolute risk estimate for developing polyps or even adenocarcinoma at the anastomotic site is still unknown. The present study showed that patients, who underwent a RPC with an IPAA, still have a substantial risk of developing adenomas.

There is little agreement among surgeons about whether a mucosectomy should be performed or not. Mucosectomy is believed to eliminate the risk for the development of polyps. Nevertheless, it has been reported that small islets of rectal mucosa may remain after a proctocolectomy with a hand-sewn pouch-anal anastomosis and a mucosectomy down to the dentate line.\textsuperscript{24,25} Furthermore, these mucosal islands remaining between the pouch and the rectal muscular cuff might contribute to postoperative pelvic sepsis.\textsuperscript{26} It is also reported that after such a mucosectomy, up to 77.5\% of the patients develop symptoms of soiling,\textsuperscript{27} especially at night.\textsuperscript{15} Others report no such difference in soiling between hand-sewn and double-stapled techniques.\textsuperscript{28,29}

A proctocolectomy with a double-stapled ileal pouch-anal anastomosis without a mucosectomy, is claimed to be safer and technically more simple than the hand-sewn technique, as the mucosectomy is omitted, thereby reducing anal canal manipulation and operating time to a minimum. This may result in better postoperative manometric and functional results.\textsuperscript{29} In addition the mucosa of the anal transitional zone just above the dentate line is preserved, which may be important for fine control of continence and the ability to discriminate between gas and stools.\textsuperscript{30} However, there is always a substantial risk that rectal mucosa is retained due to bilateral dog-ear formation at the time of the stapling of the anastomosis.\textsuperscript{10}
Our findings indicate that after both procedures a substantial risk for polyp formation remains even if a mucosectomy is performed. Therefore, patients who underwent either one of these surgical procedures need strict surveillance. However, if polyps do recur at the anastomotic site, they can be treated by local excision or an additional local mucosectomy and a pouch advancement. Nonetheless, the concern remains, that islets of mucosa between the pouch and the rectal muscular cuff after a mucosectomy and a hand-sewn anastomosis can not be checked for dysplastic changes.

A history of bowel cancer at the time of the colectomy is one of the significant risk factors for the development of a rectal carcinoma in the rectal stump in FAP patients who underwent a rectum-saving procedure with an ileo-rectal anastomosis.8 The data presented in this paper show that the presence of a synchronous colorectal carcinoma at the time of a restorative proctocolectomy with a IPAA did not significantly influence the relative risk for developing polyps at the anastomotic site.

Although our study is limited because of the varying extent of follow-up, we can conclude that there is a substantial risk for developing polyps at the anastomotic site, which can be partially, but not totally, reduced by a hand-sewn anastomosis with a mucosectomy. All FAP patients who underwent an IPAA procedure, irrespective of the applied surgical technique, should undergo endoscopic IPAA surveillance at regular intervals of at least once a year.

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References


