Functional outcome and quality of life after rectal resection
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Chapter 6

QUALITY OF LIFE AFTER TOTAL COLECTOMY WITH ILEORECTAL OR PROCTOCOLECTOMY AND ILEOANAL ANASTOMOSIS FOR FAMILIAL ADENOMATOUS POLYPOSIS


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Abstract

Background/Aims: Knowledge of post-operative health status is important in decision making about the type of operation necessary in patients with familial adenomatous polyposis (FAP). This study compares the quality of life (QOL) between patients with an ileal pouch-anal anastomosis (IPAA), and those with an ileorectal anastomosis (IRA).

Method: QOL was assessed with both a generic questionnaire, Short Form-36 Health Survey (SF-36), and a disease-specific questionnaire, Colorectal QOL Questionnaire (EORTC QLQ-CR38). The SF-36 consists of 36 items representing eight generic health domains, and the EORTC QLQ-CR38 comprises 38 items comprising disease-specific health domains. Both questionnaires were distributed among 323 FAP patients known at the Dutch Polyposis Registry who had previously undergone IRA or IPAA. The results of the SF-36 were compared to the scores of age and sex-matched respondents from the general population.

Results: 279 (86%) patients, i.e., 161 IRA and 118 IPAA patients, completed the questionnaires. Generic and disease-specific QOL was the same for IRA and IPAA patients. The SF-36 scores of both groups were significantly lower than those of the general population.

Conclusions: As the present study showed no differences regarding health status between patients with an IRA or IPAA, preference for either procedure cannot be based on QOL.
Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited disorder caused by germline mutations of the Adenomatous Polyposis Coli (APC)-gene. The disease is characterised by the development of hundreds of adenomatous polyps throughout the colorectum. Most patients develop polyps in the second and third decade of life; if these are left untreated, the patient eventually develops cancer by the age of 40.\textsuperscript{1} To date, the only effective therapy is prophylactic surgery. Until recently the most frequently used procedure was a colectomy with an ileo-rectal anastomosis (IRA).\textsuperscript{2} This procedure, which is technically relatively simple, has the advantage of a low complication rate and good functional results.\textsuperscript{3} However, a well-known disadvantage is that, due to recurrent polyps or cancer, about half of these patients need a secondary proctectomy. For this reason, an increasing number of patients are currently treated with a proctocolectomy and an ileal pouch anastomosis (IPAA), as this procedure results in a more radical removal of all colonic mucosa at risk, although there remains a risk to develop polyps at or in the pouch which does not release them from surveillance.\textsuperscript{4,6} Besides this technique being more complex, it also involves a number of disadvantages, including the incidental need for temporary diverting ileostomy (and therefore a second operation), a higher complication rate, the risk for pouch excision due to malfunction, and inferior functional results. The fact that almost half of the patients who have undergone an IRA need a secondary proctectomy\textsuperscript{7} might constitute a strong argument for the immediate choice of a more definitive procedure, i.e., IPAA. IRA would be a more appropriate procedure only if the resulting quality of life (QOL) was significantly better than that following IPAA, although in half the patients this would only be a temporary solution. Most of the published studies on QOL in FAP patients are characterised by small sample sizes and non-standardised or non-validated questionnaires.\textsuperscript{8-11} Moreover, only in a few studies was QOL regarded as the principal outcome. In these studies only one of the two surgical procedures were compared with patients with an ileostomy. The studies indicated that QOL following IPAA is most frequently reported as satisfactory or excellent,\textsuperscript{3,9,12-15} or very good in comparison to Kock pouches or Brooke ileostomies.\textsuperscript{16,17} QOL in patients who underwent an IRA is reported to be very good to excellent in 83 to 92 % of all patients.\textsuperscript{3,12,13} Our aim, therefore, was to assess the QOL with validated measures in a large series of FAP patients with either IRA or IPAA.
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Methods

Patients
In 1985, the Netherlands Foundation for the Detection of Hereditary Tumours established a registry of patients with FAP. By January 1997, the registry had collected medical and pathology data on 210 families with FAP. The families included 323 FAP patients who had undergone surgery for FAP in various medical centres between 1961 and 1996. Colectomy and IRA were performed in 183 patients, whereas 140 patients underwent IPAA. In the Netherlands, IPAA procedures had been performed in FAP patients since 1984. A questionnaire was mailed to all registered patients with an IPAA or an IRA.

An age and sex-matched sample of 279 subjects was randomly selected from a group of volunteers from the Dutch general population (n =1771), who also completed the SF-36. This group served as a control group.

Study instruments
The questionnaire included the Dutch version of the generic health related QOL questionnaire, the Medical Outcomes Study Short-Form (SF-36), and a disease-specific QOL instrument designed specifically for the evaluation of colon cancer therapy, the European Organisation for Research and Treatment of Cancer Colorectal Quality of Life Questionnaire (EORTC QLQ-CR38).

SF-36 contains 36 questions, organised into eight multi-item scales: physical functioning, role limitations owed to physical health problems, bodily pain, general health perception, vitality, social functioning, role limitations owed to emotional problems, and general mental health. In addition, SF-36 has one single-item health transition, which estimates the change in health status over the preceding year. SF-36 has previously been validated for use in postoperative patients and its reliability and validity have been established in the U.S.A. and in the Netherlands. The raw scores are linearly transformed to fit in a range from 0 to 100, with higher scores representing better levels of functioning.

The EORTC QLQ-CR38 is composed of 38 questions. Nineteen questions are completed by all patients, while the remaining 19 questions are completed by sub-samples of patients (i.e., males or females, or patients with or without a stoma). The EORTC QLQ-CR38 is subdivided into two functional scales (i.e. body image and sexual functioning), seven symptom scales (micturition problems, gastrointestinal tract symptoms, chemotherapy side effects, defecation problems, stoma-related problems, male and female sexual problems), and three single-item measures (sexual enjoyment, weight loss, and future perspective). Validity and reliability have been established in Dutch patients with colorectal cancer.
summed within scales and rescaled from 0 to 100. A higher score indicates better functioning for all functioning scales and for two of the single items, sexual enjoyment and future perspective. For all symptom scales and the remaining single item, weight loss, a higher score indicates a higher level of symptomatology.

To correct for the possible confounding effects of comorbid chronic conditions on QOL, respondents were asked if their doctor had told them they had diabetes, renal or cardiovascular diseases, chronic obstructive pulmonary disease, low back problems, arthritis, obesity, or malignancies other than colorectal cancer.

**Statistical Analysis**

For both subgroups, the SF-36 scales were compared with those of an age and sex-matched sample of the Dutch general population. Comparisons between groups were performed using univariate and multivariate analysis of variance (ANOVA or MANOVA). The effect of relevant covariates and their interactions were examined; these comprised gender, comorbidity (i.e. with at least one comorbid chronic health condition present), conversion of IRA to IPAA, age, and the length of follow-up. A $p$ value $< 0.05$ was considered statistically significant. Incomplete questionnaires were handled in accordance with the standards indicated in the respective questionnaire manuals.
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Results

Patients

The overall response rate was 86%, resulting in 279 questionnaires returned by 323 operated FAP patients. The 44 non-respondents were 22 IRA patients and 22 IPAA patients. Table 1 outlines the patient characteristics. IRA patients were significantly older and had a longer follow-up period than IPAA patients. Six IRA patients and eight IPAA patients had a permanent ileostomy. In two of these six IRA patients, an ileostomy was constructed following proctectomy for recurrence of polyps in the rectal remnant. An ileostomy was made in two other IRA patients because of recurrent distal obstruction due to irresectable desmoid tumours. Two IRA and five IPAA patients had a permanent ileostomy because of anastomotic complications. Two IPAA patients developed therapy-resistant pouch dysfunction and needed an ileostomy. In one IPAA patient the mesenteric vessels were too short to allow an ileo-anal anastomosis.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>IRA</th>
<th>IPAA</th>
<th>NR IRA</th>
<th>NR IPAA</th>
<th>Dutch Population</th>
</tr>
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<tbody>
<tr>
<td>N</td>
<td>161</td>
<td>118</td>
<td>22</td>
<td>22</td>
<td>279</td>
</tr>
<tr>
<td>Response rate (%)</td>
<td>88</td>
<td>84</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean age ± SD (yr)</td>
<td>41 ± 15</td>
<td>37 * ± 12</td>
<td>38 ± 15</td>
<td>37 ± 11</td>
<td>39 ± 14</td>
</tr>
<tr>
<td>Mean age at surgery ± SD (yr)</td>
<td>29 ± 13</td>
<td>30 ± 11</td>
<td>25 ± 10</td>
<td>26 ± 12</td>
<td></td>
</tr>
<tr>
<td>Male / Female (%)</td>
<td>48 / 52</td>
<td>57 / 43</td>
<td>61 / 39</td>
<td>77 / 23</td>
<td>51 / 49</td>
</tr>
<tr>
<td>Length of mean follow-up (yr)</td>
<td>12 ± 7.5</td>
<td>6.8 * ± 4.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of anastomosis</td>
<td>hand-sewn / double stapled (%)</td>
<td>38 / 62</td>
<td></td>
<td>63 / 37</td>
<td></td>
</tr>
<tr>
<td>Median number of control endoscopies (range)</td>
<td>1/6 months</td>
<td>1/12 months</td>
<td>(6/yr- 1/3 yr)</td>
<td>(3/yr- 1/5 yr)</td>
<td></td>
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<tr>
<td>Comorbidity present (%)</td>
<td>57</td>
<td>62</td>
<td>9</td>
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</tbody>
</table>

NR = Non Responders * p < 0.05, IRA vs. IPAA.

Questionnaire outcomes

The results derived from the SF-36 questionnaire are shown in Figure 1. The multivariate analysis showed no differences between the IRA and the IPAA patients for all subscales, (F_{9,266} = 1.7; p = 0.09). The SF-36 scores for all subscales of patients with either an IRA or IPAA were significantly poorer than those of the general population (IRA versus general population F_{9,429} = 111.9; p < 0.001, IPAA versus general population F_{9,385} = 91.8; p < 0.001).
**Figure I: The SF-36 results are expressed as mean scores and 95% (represented by error bars) for FAP patients with an ileorectal anastomosis (IRA) or an ileal pouch-anal anastomosis (IPAA) and an age- and sex-matched sample of the general population. Higher scores indicate better health status. The scores of all 9 subscales of both patients with an IRA or an IPAA were significantly worse ($p < 0.05$) than those of the healthy control group.**

Mean scores and 95% CI of the function scales and the symptom scales of the EORTC QLQ-CR38 for both patient groups are presented in Figures 2 and 3. The multivariate analysis showed a significant difference between the IRA and the IPAA patients ($F_{7,251} = 2.3; p = 0.03$). Univariate tests, however, showed that this effect was due only to the difference in defecation problems ($F_{1,258} = 6.3; p = 0.01$). As expected, more defecation problems were reported by IPAA patients than by IRA patients.

**Subanalyses**

Regarding the difference in follow-up between the two surgical groups, an additional subanalysis was performed where a subset of 93 IRA patients with the same follow-up as the patients in the IPAA group, was compared with the IPAA group. The analysis showed that there were no differences between these surgical groups for the SF-36 subscales ($F_{9,207} = 1.4; p = 0.17$), but for the EORTC-QLQ-CR38 subscales there was a significant difference ($F_{7,207} = 3.1; p = 0.04$), however, univariate analysis showed again that this difference could be
contributed to a single difference, being more defecation problems in patients with an IPAA ($F_{1,207} = 10.9; p = 0.01$).

A subsequent subanalysis was performed between 44 IPAA patients in whom the anastomosis was constructed with a double stapling technique and 71 IPAA patients in whom a hand sewn anastomosis was constructed (of 3 patients the type of anastomosis was unknown). The multivariate analysis showed no differences between patients with either type of anastomosis for both all SF-36 ($F_{9,115} = 1.1; p = 0.34$) as EORTC-QLQ-CR38 subscales ($F_{7,115} = 1.0; p = 0.47$).

**Figure 2:** The EORTC QLQ-CR38 functioning scales and the single items, sexual enjoyment and future perspective results are expressed as mean scores 95% CI (represented by error bars) for FAP patients with an ileorectal anastomosis (IRA) or an ileal pouch-anal anastomosis (IPAA). A higher score indicates better functioning.

**Covariate analysis**

Inclusion of gender, comorbidity and conversion of IRA to IPAA as covariates did not change the effects on both the SF-36 and EORTC QLQ-CR38 scores for the IRA or IPAA groups. Moreover, although the IRA and IPAA groups differed in mean age and follow-up, a covariate analysis indicated that, for the SF-36, there was no interaction between the type of operation and age ($F_{9,276} = 1.7; p = 0.09$), age at time of surgery ($F_{9,276} = 1.6; p = 0.10$) and follow-up ($F_{9,276} = 1.2; p = 0.31$). With regard to the EORTC QLQ-CR38 scores, inclusion of age and follow-up as covariates still resulted in a significant difference between the IRA and the IPAA patients; these were due to defecation problems.
Figure 3: The EORTC QLQ-CR38 symptom scales and the single weight-loss item are expressed as mean scores and 95% CI (represented by error bars) for FAP patients with an ileorectal anastomosis (IRA) or an ileal pouch-anal anastomosis (IPAA). A higher score indicates a higher level of symptomatology, $*p<0.05$, IRA vs. IPAA.

Discussion

Although several studies have shown that chemoprevention might be effective in reducing colorectal adenomas in patients with FAP, surgery is the only curative treatment available. Between their 15th and 30th years, most patients will undergo prophylactic surgery consisting of a total colectomy with ileorectal (IRA) or proctocolectomy and ileoanal anastomosis (IPAA). During this key period of life, long-term relationships are established and career plans are made. Therefore, it is important to choose an operation that interferes as little as possible with normal life, i.e., a surgical procedure with a low complication rate, the best functional results, and no mortality. These requirements are also relevant when it is considered that these patients are usually asymptomatic.

It has been reported that IRA has better functional results than IPAA.\textsuperscript{8,11} This was confirmed in a previous study where it was reported that patients who have undergone a total colectomy with an ileorectal anastomosis scored significantly better than patients who have undergone an ileal pouch-anal anastomosis for daytime and night-time stool frequency, soiling, occasional passive incontinence, flatus and faeces discrimination, stool-consistency and the need for anti-diarrheal medication. There was no difference with regard to perianal irritation, episodes
of bowel discomfort or dietary restrictions.\textsuperscript{26} This might be a reason to choose IRA as the primary treatment, although in almost half the patients, it would be only a temporary solution. It is therefore important to know whether these better functional results also bring about an improvement in QOL.

As stated above, while there are several studies on the QOL of FAP patients undergoing either type of surgery, none of these studies used standardised or validated questionnaires. Only one study\textsuperscript{10} with a small sample size (17 IRA and 7 IPAA patients) compared the QOL between patients with an IRA or IPAA, and showed no significant difference between the two surgical procedures. The results of the present study of 279 FAP patients demonstrate that, as measured by validated questionnaires, general and disease-specific QOL in IRA patients is not different from the QOL of patients who underwent an IPAA. The two groups were highly comparable except for age and the duration of follow up. Analysis of the impact of these factors and the effect of comorbidity or conversion of IRA to IPAA indicated that they did not influence the results with respect to type of operation.

This is a rather surprising finding, as it might have been expected that, in view of the worse functional outcome reported for such patients, FAP patients with an IPAA would score worse on QOL estimates.\textsuperscript{8,11} One explanation might be that the questionnaires measuring the QOL are not sensitive enough. However, the validity of the SF-36 and EORTC QLQ-CR38 questionnaires is demonstrated by their ability to discriminate between subgroups of patients who differ in clinical condition or performance status. For example, both questionnaires can differentiate between patients with a poor or good performance status, where poor performance status is defined as a Karnofsky performance score of 70 or below.\textsuperscript{18,25} Moreover, the large sample size of this study generated sufficient power to detect moderate to small differences in QOL. To estimate the capacity of the two questionnaires to detect small to moderate differences between IRA and IPAA ratings, power calculation methods as described by Cohen\textsuperscript{27} were used, where effect sizes of 0.20, 0.50 and 0.80 were considered small, medium and large, respectively. The statistical power for both questionnaires to detect small differences was 0.72, and 0.99 to detect moderate and large differences. These arguments mean that these questionnaires were sensitive enough, and the sample size large enough, to adequately pick up moderate to small differences in QOL between the two surgical procedures.

Another explanation for the relatively low QOL in IRA patients might be that these patients need frequent endoscopic examinations and are in constant fear of a recurrence of polyps or cancer in their 'time bomb' rectum. Yet another explanation might be that follow-up of both patient groups is long enough to
allow patients to have become adjusted to the poor functional results of this procedure. All these patients might thereby have undergone a 'response shift'.

This phenomenon is defined as a change in the meaning of one’s self-evaluation of QOL as a result of changes in the respondent’s internal standards, values, or conceptualisation of QOL. In other words, patients may have lowered their internal standards, altered their values and changed their ideas about what constitutes a good QOL to accommodate deteriorating function. These changes may have been more pronounced among IPAA patients to achieve a level of quality-of-life comparable to that of IRA patients.

This does not alter the fact that patients have to undergo extensive surgery. Therefore, the finding that the QOL of IRA patients is significantly poorer than that of the general population might be an argument to postpone the operation in patients with a mild phenotype of the disease. Such patients may be encountered in families with an attenuated or atypical form of polyposis.

To get a valid assessment of short-term QOL and the development of QOL in time a prospective study should be performed, however, on the basis of these results, a difference in QOL cannot be used as an argument in the choice between IRA and IPAA. Therefore, we recommend IPAA for FAP patients with a high risk of secondary surgery, i.e., a severe phenotype, and reserve IRA only for patients with a mild phenotype and therefore a low risk of secondary proctectomy. The remaining problem is how to identify patients with a low risk of secondary proctectomy. Two recent studies have shown a high correlation between mutation site and the risk of secondary surgery. It is reported that families with polyposis due to mutations located in a region on the APC gene between codon 1250 and 1462, especially mutations at codon 1309 or 1328, are predisposed to develop a severe phenotype and have a higher risk of rectum excision. If these results are confirmed by studies with larger numbers of patients, this information might be used in the surgical decision making.

References


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