Functional outcome and quality of life after rectal resection
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DECISION ANALYSIS IN THE SURGICAL TREATMENT OF FAMILIAL ADENOMATOUS POLYPOSIS: A DUTCH-SCANDINAVIAN COLLABORATIVE STUDY ON 659 POLYPOSIS PATIENTS

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Abstract

Background/Aims: The choice of surgery in patients with familial adenomatous polyposis lies between the morbidity of proctocolectomy and ileum pouch-anal anastomosis (IPAA) and the mortality from rectal carcinoma after total colectomy and ileorectal anastomosis (IRA). The aims of the present study were: (1) to assess the risk of dying from rectal carcinoma after IRA, (2) to compare the life expectancy between patients with an IRA and those with an IPAA and (3) to investigate whether regular endoscopic examination leads to detection of carcinoma at an earlier stage.

Methods: Clinical and pathological data on 659 patients who underwent total colectomy and ileorectal anastomosis were collected from four National Polyposis Registries, i.e., in Denmark, Finland, Sweden and the Netherlands. The data were analyzed using survival analysis methods. Decision analysis was used to compare the life expectancy between patients with an IRA and those with an IPAA.

Results: A total of 47 patients developed rectal carcinoma after IRA. The risk of dying from rectal carcinoma was 12.5 percent (CI: 7.1-17.9%) by age 65. Compared to IRA, IPAA would lead to an increase in life expectancy of 1.8 years. Seventy-five percent of the patients with rectal carcinoma had a negative endoscopy within 12 month before diagnosis.

Conclusions: IRA is associated with a substantial mortality due to rectal carcinoma. Follow up examinations of the rectum do not guarantee early detection of rectal carcinoma.
Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant disease characterized by the development of numerous adenomas in the colorectum and various other extracolonic manifestations such as adenomas in the upper GI tract, desmoids and retinal lesions. 1 The syndrome is caused by mutations in the APC (Adenomatous Polyposis Coli) gene. 2,3 Most patients develop colorectal adenomas in their second decade of life. If they are not timely treated, they will develop colorectal carcinoma in the third and fourth decade of life. 1 The establishment of Polyposis Registries in various countries encouraged genealogical studies in FAP families and, consequently, the identification of family members at risk for the disease. 4 These activities led to the detection of polyposis at an earlier, often pre-malignant stage 5,6 and to improvement of the prognosis. 7 Although medical treatment, e.g. sulindac is effective in reducing the number and/or size of the adenomas, 8-10 the only curative treatment of colonic polyposis is still surgical. Until a decade ago, colectomy with an ileorectal anastomosis (IRA) was the most frequently applied surgical procedure for patients with polyposis. This surgical option is attractive because it is a relatively simple procedure with good functional results. A major disadvantage of the procedure, however, is the need for continuous endoscopic follow up and the risk of rectal carcinoma that increases over time. 11,12 In addition, in about half of the cases a secondary proctectomy is needed because of uncontrollable polyps. 12 These disadvantages might be the reason that an increasing number of patients is treated with the alternative surgical option, i.e., a proctocolectomy and ileoanal anastomosis (IPAA). However, this surgical procedure has also various disadvantages including a risk of severe postoperative complications, in the worst case necessitating removal of the pouch and construction of an ileostomy. Another disadvantage is the inferior functional outcome as compared to that after IRA. 13 For patients with a large number of rectal adenomas or rectal carcinoma and patients that will not comply to follow up examinations after IRA, an IPAA seems the procedure of first choice. There is, however, no agreement about the best surgical option for patients with only a few or no rectal adenomas. In the decision making between the two procedures the risk of developing rectal carcinoma after IRA is important but even more crucial is the risk of dying of rectal carcinoma.

The aims of the present study are, therefore, to assess the risk of dying from rectal carcinoma in a large series of IRA patients, and to find out whether frequent follow up of the rectum leads to the detection of rectal carcinoma at an early stage. In addition, using the technique of decision analysis, we evaluated
whether there is a difference in life expectancy between the two surgical procedures.

Patients and Methods

Four national polyposis registries, i.e., in Finland, Denmark, Sweden and The Netherlands participated in the study. Clinical information was collected on 659 patients who underwent a colectomy with an ileorectal anastomosis for FAP between 1940 and 1997. The registered data included information on the mode of diagnosis, the age at diagnosis, pathology, age at surgery, type of surgery, age at death and causes of death. Hundred-ninety-three of the 659 patients (29%) presented with symptoms and 418 patients (63%) were identified by family screening. For the remaining patients the mode of diagnosis is not known.

For risk assessment, patients who underwent an IRA were studied with respect to their risk of dying due to rectal carcinoma. The data were analyzed using survival analysis methods. Observation time was from the date of surgery up to the date of last contact, death, the date of rectal excision for other reasons or closing date of the study, i.e., the first of January 1997.

![Decision tree for comparing life expectancy between patients with an IRA and those with an IPAA.](image)

Figure 1: Decision tree for comparing life expectancy between patients with an IRA and those with an IPAA.
A decision model was developed to estimate the potential health effects (life expectancy) of the two surgical options. The calculations were applied to a hypothetical polyposis patient aged 25 years who was found to have hundreds of adenomas in the colon and only a few in the rectum. The age of 25 years was chosen because the mean age at surgery is about this age. The first step was to identify the outcomes of both surgical options and to construct a decision tree displaying these events in their proper time sequence. The decision model for both strategies is shown in Figure 1. Points where the tree branches (“nodes”) are indicated by a square when they are under the control of the physician and by a round symbol when they are not. The software program “Decision maker” was used to calculate the life expectancies.

Results

Table 1: Mortality observed in patients with IRA

<table>
<thead>
<tr>
<th>Cause</th>
<th>Screen-detected group</th>
<th>Total group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Rectal carcinoma after IRA</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td>Non FAP-related</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Duodenal carcinoma</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Other carcinoma</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Metastatic primary colorectal carcinoma</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

Ninety-seven patients died at a mean age of 48 years (21-80 yrs). The main cause of death in the total group of patients was metastatic colorectal carcinoma. In the screen-detected group rectal carcinoma was the main cause of death. The causes of death are listed in Table 1. A total of 47 patients developed rectal carcinoma after IRA. The mean age at diagnosis of rectal carcinoma was 44.5 (range: 21-46 years). The Dukes stages of the tumors are shown in Table 2.

Table 2: Comparison of Dukes stages between patients with rectal carcinoma after IRA and patients with sporadic colorectal carcinoma.

| Dukes stages | Rectal carcinoma after IRA | Sporadic colorectal carcinoma
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>A</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>B</td>
<td>19</td>
<td>40</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>
Dukes A carcinomas were more frequently observed among patients with rectal carcinoma after an IRA than in patients with sporadic colorectal carcinoma registered at the Dutch Cancer Registry. Seventy-five percent of the patients had a negative endoscopic examination within one year before diagnosis of the carcinoma. The majority of these patients (19 out of 28) had Dukes stage A or B colorectal carcinoma (Table 3).

Table 3: Interval since last negative endoscopy in patients diagnosed with rectal carcinoma

<table>
<thead>
<tr>
<th>Months</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 6</td>
<td>13*(35%)</td>
</tr>
<tr>
<td>6 – 12</td>
<td>15**(40%)</td>
</tr>
<tr>
<td>12 – 18</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>18 – 24</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>&gt; 24</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
</tr>
</tbody>
</table>

Two Dukes A, eight Dukes B, one Dukes C carcinomas and two colorectal carcinomas with distant metastases; ** Two Dukes A, seven Dukes B, four Dukes C and two colorectal carcinomas with distant metastases.

The 10 years survival according to the various pathological stages is shown in Figure 2. The risk of dying from rectal carcinoma was 8% by age 55, 9% by age 60 and 12.5% (CI: 7.1%-17.9%) by age 65. The probabilities of dying from rectal carcinoma for patients operated before and after 1980 were 7% and 6% at 10 years after surgery, respectively.

Figure 2: Survival of patients with rectal carcinoma according to Dukes' stages A-D.
A summary of the data used in the decision analysis is shown in Table 4. The assessment of the risk of developing rectal carcinoma or the risk of a secondary proctectomy for other reasons is subject of a recent study from our group. The estimated risk of a secondary proctectomy because of rectal carcinoma found in this study is 26% by age 65 years and the estimated risk of a secondary proctectomy for other reasons was 34% by age 65 years. The mean age of the patients in this study at time of proctectomy because of rectal carcinoma or because of other reasons was 45 respectively 36 years.

Table 4: Data used for the decision analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk proctectomy rectal carcinoma by age 65</td>
<td>26%</td>
</tr>
<tr>
<td>Risk proctectomy other reasons by age 65</td>
<td>34%</td>
</tr>
<tr>
<td>Mean age proctectomy rectal carcinoma</td>
<td>45 years</td>
</tr>
<tr>
<td>Mean age proctectomy for other reasons</td>
<td>36 years</td>
</tr>
<tr>
<td>Peri-operative mortality</td>
<td>0.005</td>
</tr>
<tr>
<td>Risk metastatic rectal carcinoma</td>
<td>0.39</td>
</tr>
<tr>
<td>10-yrs survival local rectal carcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>10-yrs survival metastatic disease</td>
<td>25%</td>
</tr>
<tr>
<td>Life expectancy 25-years-old FAP patient</td>
<td>45 years</td>
</tr>
</tbody>
</table>

The life expectancy of males and females at birth in the Netherlands and the Scandinavian countries is 75 and 80 years, respectively (on average 77 years). We assumed that the life expectancy of a patient with polyposis is shortened by 7 years because of death due to extracolonic lesions such as desmoid tumors and duodenal carcinomas. Hence, the life expectancy of a hypothetical 25 years-old polyposis patient is 45 years. As reports on development of carcinoma after IPAA are very rare, we assumed that this risk might be neglected. If all parameters are entered in the decision model, an increase of life expectancy of 1.8 years is found for a proctocolectomy followed by IPAA.

Discussion

The present study revealed that patients with an IRA have a substantial higher risk of dying from rectal carcinoma than has been suggested earlier. In contrast with studies, that showed that desmoid tumors and duodenal carcinomas are the most frequent causes of death in screen-detected cases, in the present study rectal carcinoma was the most frequent cause of death in this group. The development of rectal carcinoma can not be attributed to failure of compliance as 75 percent of the patients had an endoscopic examination within 12 months before the diagnosis of rectal carcinoma. Although periodic examination led to detection of more Dukes A carcinomas, it certainly did not prevent the
development of advanced stages of rectal carcinoma. Using decision analysis we
found that IPAA led to increase of life expectancy by 1.8 years. We did not
adjust the life expectancies for quality of life as a recent study from our group did
not reveal any differences in quality of life between IRA and IPAA.\textsuperscript{17}
For the analysis we assumed that the risk of developing carcinoma from residual
rectal mucosa after IPAA might be neglected. In this respect, it should be noticed
that a recent international collaborative study revealed that patients with an IPAA
have a significant risk of adenoma especially after a double stapled procedure.
Reports of carcinomas that developed after IPAA in the literature are very
rare,\textsuperscript{18,19} but the follow up after this surgical procedure is still short (15-20 years).
In addition, adenomas in the pouch have been reported.\textsuperscript{20} One study reported
adenomas in the ileal pouch in 11 (42\%) out of 26 patients.\textsuperscript{21}
The current study included patients who underwent surgery over a long period of
time (1940-1997). In the course of time, indications for surgery might have been
changed. Patients with a moderate number of rectal polyps will currently be
selected for an IPAA procedure while in the past such patients might probably
have been selected for IRA instead of the only alternative at that time, i.e.,
proctocolectomy with an ileostomy. As a consequence the risk of carcinoma in
patients that nowadays are selected for IRA might be lower than the risk in
patients selected for an IRA 20 years ago. A subanalysis, however, showed no
significant difference in risk of dying from rectal carcinoma between patients
who underwent surgery before and those with surgery after 1980 (the time since
IPAA is widely applied).
An alarming finding in the present study is that follow up examinations and
polypectomies do not guarantee early detection of rectal carcinoma. The question
is how the effectiveness of endoscopic surveillance in this group of patients can
be improved. Nugent suggested in selected cases to shorten the interval between
examinations from six to four months.\textsuperscript{22} Another possibility is to use the
technique of fluorescence endoscopic imaging to identify nonpolypoid
adenomatous areas in the rectal mucosa.\textsuperscript{23} Several studies showed that sulindac
treatment lead to disappearance or reduction in size of rectal adenomas. On the
other hand patients have been reported that developed carcinoma under sulindac
treatment.\textsuperscript{24,25} Long-term follow up studies are, therefore, needed to assess
whether also the risk of carcinoma development is decreased. Until such studies
are available frequent follow up of the rectum should continue also in patients in
which the adenomas disappeared after sulindac treatment.
The results of the present study can be used in the decision making of surgical
management. The finding of a significant risk of dying from rectal carcinoma and
the shortened life expectancy can be considered as arguments against performing
IRA in patients also in those with a moderate or low number of rectal adenomas. Probably the remaining appropriate indication for an IRA procedure is a patient with a few or no rectal adenomas from a family with a similar mild phenotype of the disease.

References
