Decision analysis in the surgical treatment of patients with familial adenomatous polyposis: a Dutch-Scandinavian collaborative study including 659 patients

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Abstract

Background and aims—The choice of colorectal surgery in patients with familial adenomatous polyposis lies between the morbidity of proctocolectomy and ileum-pouch-anal anastomosis (IPAA) and the mortality from rectal cancer after total colectomy and ileorectal anastomosis (IRA). The aims of the present study were: (1) to assess the risk of dying from rectal cancer 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 of the rectum leads to detection of cancer at an earlier stage.

Methods—Clinical and pathological data on 659 patients who underwent colectomy and ileorectal anastomosis were collected from four national polyposis registries—that is, in Denmark, Finland, Sweden, and the Netherlands. Data were analysed 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 cancer after IRA. The risk of dying from rectal cancer was 12.5% (95% confidence interval 7.1–17.9%) by age 65. Compared with IRA, IPAA would lead to an increase in life expectancy of 1.8 years. Seventy five per cent of patients with rectal cancer had a negative rectoscopy within 12 months before the diagnosis.

Conclusion—IRA is associated with substantial mortality due to rectal cancer. Follow up examinations of the rectum does not have sufficient preventive effect on morbidity and mortality of rectal cancer.

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Keywords: familial adenomatous polyposis; decision analysis; colorectal surgery

Familial adenomatous polyposis (FAP) is an autosomal dominant disease characterised by the development of numerous adenomas in the colorectum and various other extracolonic manifestations, such as adenomas in the upper gastrointestinal 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 and if not treated promptly, they will develop colorectal cancer in the third and fourth decades of life.¹ The establishment of polyposis registries in various countries encouraged genealogical studies in FAP families and, consequently, identification of family members at risk for the disease.⁴ These activities led to the detection of polyposis at an earlier, often premalignant stage,^{5,6} and to improvement in prognosis.⁷

Although medical treatment with non-steroidal anti-inflammatory drugs (NSAIDs) is effective in reducing the number and/or size of the adenomas,^{8–11} the only curative treatment of colonic polyposis is surgical. Until a decade ago, colectomy with an ileorectal anastomosis (IRA) was the most frequently used surgical procedure for the treatment of FAP. This surgical option is attractive because it is a relatively simple procedure with good functional results. However, a major disadvantage is the need for continuous endoscopic follow up and the remaining risk of rectal cancer that increases over time.^{12–14} In addition, in a significant number of cases a secondary proctectomy is needed because of uncontrollable polyposis.^{14,15}

These disadvantages may be the reason that an increasing number of patients are treated with the alternative surgical option—that is, proctocolectomy and ileal-pouch-anal anastomosis (IPAA). However, this surgical procedure also has 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 poorer functional outcome compared with IRA.¹⁶

For patients with a large number of rectal adenomas or rectal cancer and those who will not comply with follow up examinations after IRA, an IPAA seems the procedure of first choice. However, there is no agreement on the best surgical option for patients with a limited number of rectal adenomas. In deciding between the two procedures, the risk of developing rectal cancer after IRA is important but even more crucial is the risk of dying of rectal cancer.

Abbreviations used in this paper: IPAA, ileum-pouch-anal anastomosis; IRA, ileorectal anastomosis; FAP, familial adenomatous polyposis; NSAIDs, non-steroidal anti-inflammatory drugs.

The aims of the present study therefore were to assess the risk of dying from rectal cancer in a large series of IRA patients and to determine if frequent follow up of the rectum leads to detection of rectal cancer 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.

Methods

Four national polyposis registries (in Finland, Denmark, Sweden, and the Netherlands) participated in the study. Clinical information was collected on 659 patients who underwent a colectomy with an IRA for FAP between 1940 and 1997. The registered data included information on the mode of diagnosis, age at diagnosis, pathology, age at surgery, type of surgery, age at death, and causes of death. A total of 193 of 659 patients (29%) presented with symptoms (probands) and 418 patients (63%) were identified by family screening (call up cases). For the remaining patients the mode of diagnosis was not known.

For risk assessment, patients who underwent an IRA were studied with respect to their risk of dying due to rectal cancer. Data were analysed 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 (31 December 1997).

A decision model was developed to estimate the potential health effects (life expectancy) of the two surgical options. 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. Age 25 years was chosen because this

is approximately the mean age at surgery. The first step was to identify the outcomes of both surgical options and to construct a decision tree displaying these events in their correct time sequence. The decision model for both strategies is shown in fig 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 life expectancies.

Results

MORTALITY

Ninety seven patients died at a mean age of 48 years (range 21–80). The main cause of death in the total group of patients was metastatic colorectal cancer. In the screen detected group, rectal cancer was the main cause of death. The causes of death are listed in table 1. A total of 47 patients developed rectal cancer after IRA. Mean age at diagnosis of rectal cancer was 44.5 years (range 21–46). Dukes' stages of the tumours are shown in table 2. Dukes' A cancers were more frequently observed among patients with rectal cancer after an IRA than in patients with sporadic colorectal cancer registered at the Dutch Cancer Registry.¹⁷ Twenty eight (75%) patients had no evidence of cancer at the previous endoscopic examination within one year before a diagnosis of rectal cancer. The majority of these patients (19 of 28) had Dukes' stage A or B colorectal cancer (table 3). Five year survival for patients with Dukes' A tumours (n=8) was 100%, for patients with Dukes' B tumours (n=19) 83%, for patients with Dukes' C tumours (n=12) 75%, and the five year survival for patients with distant metastases (n=5) was 20%. The risk of dying from rectal cancer was 8% by age 55, 9% by

Figure 1 Decision tree for a 25 year old patient with familial adenomatous polyposis.

Table 1 Mortality observed in 659 patients with ileorectal anastomosis (IRA)

Cause of death	Screen detected group		Total group	
	n	%	n	%
Rectal cancer after IRA	12	2.9	28	4
Non-FAP related	6	1.4	17	2.6
Duodenal cancer	4	0.9	8	1.2
Other cancer	4	0.9	10	1.5
Postoperative complications	2	0.4	4	0.6
Metastatic primary colorectal cancer	0	0	22	3.3
Unknown	2	0.4	8	1.2

FAP, familial adenomatous polyposis.

Table 2 Comparison of Dukes' stages between patients with rectal cancer after ileorectal anastomosis (IRA) and patients with sporadic colorectal cancer

Dukes' stage	Rectal cancer after IRA		Sporadic colorectal cancer (%) [*]
	n	%	
A	8	17	8
B	19	40	43
C	12	25	22
Distant metastases	5	11	12
Unknown	3	6	13

^{*}Data from the Dutch Cancer Registry.¹⁵

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

Time (months)	No patients (%)
0–6	13 (35) [*]
6–12	15 (40) ^{**}
12–18	5 (13)
18–24	1 (3)
>24	3 (8)
?	10
Total	47

^{*}Two Dukes' A, eight Dukes' B, one Dukes' C cancers, and two colorectal cancers with distant metastases.^{**}Two Dukes' A, seven Dukes' B, four Dukes' C, and two colorectal cancers with distant metastases.

age 60, and 12.5% (95% confidence interval 7.1–17.9%) by age 65. The probabilities of dying from rectal cancer for patients operated on before and after 1980 were 5.1% and 2.1% at 10 years after surgery, respectively.

DECISION ANALYSIS

A summary of the data used in the decision analysis is shown in table 4. Assessment of the risk of developing rectal cancer or the risk of a secondary proctectomy for other reasons was the subject of a previous study performed by the Dutch-Scandinavian collaborative group. This analysis indicated that the estimated risks of a secondary proctectomy because of rectal cancer or because of other reasons by age 65 years were 26% and 34%, respectively.¹⁸

Mean ages at proctectomy because of rectal cancer or other reasons were derived from the current data. The life expectancy of males and females at birth in the Netherlands and Scandinavian countries is 75 and 80 years, respectively (mean 77 years). We assumed that the life expectancy of a patient with polyposis is shortened by seven years because of death due to extracolonic lesions such as desmoid tumours and duodenal cancers.¹⁹ Hence the life expectancy of a hypothetical 25 year old polyposis patient is 45 years. As reports on the development of cancer in the pouch after IPAA are rare, we assumed that this risk was negligible.

Table 4 Data used for the decision analysis

- Risk proctectomy rectal cancer by age 65=0.26
- Risk proctectomy other reasons by age 65=0.34
- Mean age proctectomy for rectal cancer=45 years
- Mean age proctectomy for other reasons=36 years
- Perioperative mortality=0.005³²
- Risk local rectal cancer=0.61
- Risk metastatic rectal cancer=0.39
- 10 year survival local rectal cancer=0.90
- 10 year survival metastatic disease=0.25
- Life expectancy 25 year old FAP patient=45 years
- Risk of pouch excision after IPAA≤0.05^{16 33}

IPAA, ileum-pouch-anal anastomosis; FAP, familial adenomatous polyposis.

Using these data, we calculated the life expectancy for each patient. For example, the life expectancy of our 25 year old patient if he develops local rectal cancer is: 20 years+(0.90×25 years)+(0.10×5 years)=43 years. We then worked our way back through the decision tree by “folding it back” from right to left. By multiplying the life expectancy by the probabilities of their occurrence and summing them for each node, we could assign life expectancies to the various nodes. For example, the life expectancy for chance node A2 (37.9 years) was the life expectancy of a patient with local cancer (43 years) times the probability of presenting with this state (0.61) plus the life expectancy of a patient with metastatic cancer (30 years) times the probability of presenting with such a stage (0.39). We found that the option of IPAA would lead to an increase in life expectancy of 1.8 years.

Discussion

The present study revealed that patients with an IRA have a higher risk of dying from rectal cancer than has been suggested previously.¹² In contrast with other studies^{19 20} that showed that desmoid tumours and duodenal cancers are the most frequent causes of death in screen detected cases, in the present study rectal cancer was the most frequent cause of death in this group. Interestingly, none of the patients with an IRA in the combined series died from a desmoid tumour. The high incidence of rectal cancer cannot be attributed to failure of compliance as 75% of patients had undergone an endoscopic examination within 12 months prior to the diagnosis of rectal cancer. Although periodic examination led to detection of more Dukes' A cancers compared with symptomatic sporadic colorectal cancer, it did not prevent the development of advanced stages of rectal cancer. Using decision analysis we found that IPAA would lead to an increase in life expectancy of 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.²¹

For the analysis we assumed that the risk of developing cancer from residual rectal mucosa after IPAA was negligible. In this respect it should be noted that a recent international collaborative study revealed that patients with an IPAA have a significant risk of adenoma, especially after a double stapled procedure.²² Reports of cancers that developed after IPAA in the literature are rare^{23–26} but follow up after

Figure 2 Number of Dutch patients who underwent ileorectal anastomosis (IRA) or ileum-pouch-anal anastomosis (IPAA) over the past five decades.

this surgical procedure is still relatively short (15–20 years). Also, adenomas in the pouch have been reported similar to adenomas above the anastomosis after IRA.²⁷ One study reported adenomas in the ileal pouch in 11 (42%) of 26 patients.²⁸

The current study included patients who underwent surgery over a long period of time. Since the introduction of IPAA in 1980 an increasing number of patients are selected for this procedure (fig 2). Over the course of time the indications for surgery may have changed. Today, patients with a moderate number of rectal polyps would probably be selected for an IPAA procedure while in the past such patients would have undergone IRA rather than the only alternative at that time (that is, proctocolectomy with a rather mutilating ileostomy). As a consequence, the risk of cancer in patients that are now selected for IRA (patients with a relatively mild polyposis) may be lower than the risk in patients selected for an IRA 20 years ago. Indeed, a subanalysis showed a higher risk of dying from rectal cancer in patients who underwent surgery before 1980 (risk 5.1% at 10 years after surgery) compared with those with surgery after 1980 (risk 2.1% at 10 years after surgery).

A striking finding in the present study was that follow up examinations and polypectomies did not prevent the development of cancer. The question is, how can the effectiveness of endoscopic surveillance of the rectum in this group of patients be improved? The increasing use of flexible sigmoidoscopy instead of rigid rectoscopy may improve early detection of rectal cancer. Nugent and Phillips suggested shortening the interval between examinations from six to four months in selected cases.¹³ Another possibility is to use the technique of fluorescence endoscopic imaging to identify non-polypoid adenomatous areas in the rectal mucosa.²⁹ Several studies showed that treatment with NSAIDs leads to disappearance or reduction in the size of rectal adenomas. On the other hand, patients who developed cancer while receiving sulindac treatment have been reported.^{30–31} Long term follow up studies are needed to assess if the risk of cancer development is decreased by treatment with NSAIDs. Until such studies are available frequent follow up of the rectum should also continue in patients in which the adenomas disappeared after treatment.

The results of the present study can be used in the decision making of surgical management. The significant mortality due to rectal cancer after IRA and the shortened life expectancy after IRA compared with IPAA can be considered arguments against IRA. Probably the only appropriate indication for an IRA procedure is a patient with few or no rectal adenomas from a family with a similar mild phenotype of the disease.

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