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Abstract

Background—Patients with familial adenomatous polyposis are not only at high risk of developing adenomas in the colorectum but a substantial number of patients also develop polyps in the duodenum. Because treatment of duodenal polyps is extremely difficult and it is unknown how many patients ultimately develop duodenal cancer, the value of surveillance of the upper digestive tract is uncertain.

Aims—(1) To assess the cumulative risk of duodenal cancer in a large series of polyposis patients. (2) To develop a decision model to establish whether surveillance would lead to increased life expectancy. Methods—Risk analysis was performed in 155 Dutch polyposis families including 601 polyposis patients, and 142 Danish families including 376 patients. Observation time was from birth until date of last contact, death, diagnosis of duodenal cancer, or closing date of the study.

Results—Seven Dutch and five Danish patients developed duodenal cancer. The lifetime risk of developing this cancer by the age of 70 was 4% (95% confidence interval 1–7%) in the Dutch series and 3% (95% confidence interval 0–6%) in the Danish series. Decision analysis showed that surveillance led to an increase in life expectancy by seven months.

Conclusions—Surveillance of the upper digestive tract led to a moderate gain in life expectancy. Future studies should evaluate whether this increase in life expectancy outweighs the morbidity of endoscopic examination and proximal pancreaticoduodenectomy.

Keywords: familial adenomatous polyposis, duodenal cancer, surveillance, decision analysis, pancreaticoduodenectomy.
development of duodenal cancer from birth until death. The data were analysed by life table analysis methods. Observation time was until date of last contact, death, date of diagnosis of a duodenal cancer, or closing date of the study, 31 December 1995.

DECISION ANALYSIS

We applied the technique of decision analysis to a hypothetical male polyposis patient, 30 years of age, who had undergone colectomy and ileorectal anastomosis. The first step was to identify all the alternative actions, treatments, and outcomes that could occur for the patient in question. On the basis of this, a decision model (shown in the Figure) that displays these elements in their proper time sequence was developed. Points where the tree branches (“nodes”) are square (“choice nodes”) when they imply a decision under the control of the physician, and round (“chance nodes”) if a chance outcome occurs.

Results

RISK ANALYSIS

On 31 December 1995, the Dutch Polyposis Register included about 200 families with FAP. Data collection was completed in the first 155 families and these families were selected for the present study. The 155 families included 711 patients with FAP. The diagnosis of FAP was confirmed by pathology and/or medical reports in 601 patients. One hundred and eighteen patients died; the cause of death is known in 91% of the patients. Among the 601 patients, seven developed duodenal cancer (including one suspected case). The mean age at diagnosis of duodenal cancer was 47 years (range 39–53). The cumulative risk of developing duodenal cancer by age 70 was 4% (95% confidence interval 1–7%). The number of patients at risk by age 70 was 27.

On 31 December 1995, the Danish Polyposis Register included 142 FAP families with a completed data collection, including 454 patients of whom 376 had a histologically verified FAP. The cause of death is known for all 160 deceased patients. In five patients data were insufficient. Of the remaining 371 affected patients, five developed duodenal cancer; the mean age at diagnosis was 51 years (range 43–77). The cumulative risk of developing duodenal cancer by age 70 was 3% (95% confidence interval 0–6%). The number of patients at risk by age 70 was nine.
summing them for each branch, we could probabili-
ties of occurrence of each option, and left. By multiply-
ing the life expectancy by the life expectancy of the hypo-
thetical patient who develops duodenal cancer is esti-
mated at two years.

The life expectancy of a patient who develops duodenal cancer, stage IV duodenal adenomatosis, and the risk of perioperative mortality due to pancreaticoduodenotomy – were varied over a plausible range to assess their impact on the outcome of the model (Table II). The probability of developing duodenal cancer appeared to be the most important variable.

**Discussion**

After the realisation that a majority of patients with polyposis develop adenomas in the duodenum, many investigators recommended surveillance of the upper GI tract. However, before establishing such a surveillance programme, a more critical evaluation of the pros and cons of surveillance should be performed. In particular, the difficulties for effective treatment posed by duodenal adenomas make the benefit of surveillance of the upper GI tract questionable.

In the assessment of population screening, the criteria formulated by Wilson and Jungner are usually applied. These criteria are also appropriate in the assessment of surveillance of high risk groups such as patients with polyposis. According to these criteria, the natural history of duodenal adenomas should be known, a curative treatment should be available, and there should be evidence that early treatment leads to an improved prognosis.

With respect to the natural history of duodenal adenomas, the most urgent question is “do the duodenal polyps have the same malignant potential as the colonic polyps?” Earlier studies indicated that the relative risk of duodenal cancer in FAP was very high, but such information is less useful in the decision making process, because the incidence of duodenal cancer in the general population is extremely low. Much more important would be to know the lifetime risk of developing duodenal cancer. The present study revealed that the cumulative risk of duodenal cancer was less than 5% by the age of 70. Although prospective studies are needed to confirm our findings, such studies have the disadvantage that the screening examinations will inevitably lead to early detection of premalignant disease and to early surgical intervention, which will interfere with the assessment of the duodenal cancer risk.

The treatment of duodenal adenomas in our patients is limited by a number of factors. Endoscopic snaring may be made impossible by the presence of large numbers of polyps or by the usual sessile nature of the polyps. Endoscopic electrocoagulation, if repeated very often, will lead to considerable scarring, which in the periampullary area might cause strictures. Laser ablation of polyps via the endoscope can be used, but carries the risk of duodenal perforation. Polyp removal by (surgical) duodenotomy consisting of submucosal infiltration and local excision of all polyps is not

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**Table I** Classification of duodenal adenomas according to Spigelman

<table>
<thead>
<tr>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>&lt;4</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Size (mm)</td>
<td>0–4</td>
<td>5–10</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Histology</td>
<td>Tubular</td>
<td>Tubulo-villous</td>
<td>Villous</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Spigelman stage I: 1–4; stage II: 5–6; stage III: 7–8; stage IV: 9–12 points.

One analysis was conducted at the St Mark’s Polyposis Registry in London and the other in five European countries. The British study showed that 11 (11%) out of 102 FAP patients had stage IV duodenal polyposis. In the European multicentre study, 27 patients out of 310 (9%) had stage IV duodenal polyposis. In the multicentre study, 7% of the patients aged between 20 and 40 years, and 11% of those aged between 40 and 60 years had stage IV duodenal adenomatosis (personal communication, S Bülow). The cumulative risk of developing stage IV adenomatosis is therefore at least 11%. The mean age of the patients identified with Spigelman stage IV was 51 years in the British study and 38 years in the multicentre study. On these grounds we estimated that the average age of patients who reached stage IV duodenal polyposis would be 45 years. If a pancreaticoduodenotomy is performed and the patient dies as a result of complications of this procedure, the average life expectancy of a 30 year old patient would amount to 15 years. The perioperative mortality of pancreaticoduodenectomy has declined during the past decade and is now about 5%.

The cumulative risk of duodenal cancer by age 70 in the present series is 3–4%. The mean age at diagnosis of duodenal cancer in this study and in three others was about 50 years. The life expectancy of a patient who develops duodenal cancer is estimated at two years. Hence, the life expectancy of the hypothetical 30 year old patient is on average 22 years if he develops duodenal cancer.

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 occurrence of each option, and summing them for each branch, we could assign life expectancies to the various nodes. The calculations showed that the option of surveillance led to an increase in life expectancy by seven months. The key variables – the cumulative risk of stage IV duodenal adenomatosis, duodenal cancer, and the risk of mortality due to pancreaticoduodenotomy – were varied over a plausible range to assess their impact on the outcome of the model (Table II). The probability of developing duodenal cancer appeared to be the most important variable.

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**Table II** The impact of various probabilities of developing duodenal cancer, stage IV duodenal adenomatosis, and perioperative mortality on life expectancy

<table>
<thead>
<tr>
<th>Probability of duodenal cancer (%)</th>
<th>Life expectancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>39·9</td>
</tr>
<tr>
<td>10</td>
<td>39·9</td>
</tr>
<tr>
<td>15</td>
<td>39·6</td>
</tr>
<tr>
<td>Probability of stage IV duodenal adenomatosis (%)</td>
<td>Life expectancy (%)</td>
</tr>
<tr>
<td>11</td>
<td>39·9</td>
</tr>
<tr>
<td>15</td>
<td>39·6</td>
</tr>
<tr>
<td>20</td>
<td>39·7</td>
</tr>
<tr>
<td>Probability of perioperative mortality (%)</td>
<td>Life expectancy (%)</td>
</tr>
<tr>
<td>4</td>
<td>39·9</td>
</tr>
<tr>
<td>6</td>
<td>39·8</td>
</tr>
</tbody>
</table>

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**Endnotes**

13. Spigelman14
14. The British study showed that 11 (11%) out of 102 FAP patients had stage IV duodenal polyposis. In the European multicentre study, 27 patients out of 310 (9%) had stage IV duodenal polyposis. In the multicentre study, 7% of the patients aged between 20 and 40 years, and 11% of those aged between 40 and 60 years had stage IV duodenal adenomatosis (personal communication, S Bülow). The cumulative risk of developing stage IV adenomatosis is therefore at least 11%. The mean age of the patients identified with Spigelman stage IV was 51 years in the British study and 38 years in the multicentre study. On these grounds we estimated that the average age of patients who reached stage IV duodenal polyposis would be 45 years. If a pancreaticoduodenotomy is performed and the patient dies as a result of complications of this procedure, the average life expectancy of a 30 year old patient would amount to 15 years. The perioperative mortality of pancreaticoduodenectomy has declined during the past decade and is now about 5%.

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recommended, because a recent study has shown recurrence in all patients treated by this technique within a short time.\(^2^1\) To summarise, the only curative treatment appears to be a proximal pancreaticoduodenectomy. Such an operation has considerable potential morbidity and mortality which makes the indication for and the timing of surgery extremely difficult. Criteria of size, rapid growth, polyip induration, or consistently severe dysplasia or villous change suggest that intervention is necessary.

In the above mentioned British study, among the 10 patients with stage IV adenomatosis at the first endoscopy, one developed duodenal cancer and two other patients are suspected of having this type of cancer.\(^2\) Thus surgery may be considered in patients that consistently have stage IV duodenal adenomatosis.

Evidence that early treatment leads to improvement of the prognosis is not yet available, and it will probably take a long time to collect such information. The best way to demonstrate the probability of surveillance would be by randomised controlled studies showing a higher survival rate. Such studies will, however, be difficult to carry out in view of the extremely high risk of premalignant duodenal disease. Therefore, we decided to apply decision analysis to predict whether surveillance might lead to an increase in life expectancy. The calculations showed that surveillance increased the life expectancy by seven months if surgery was performed after detection of stage IV adenomatosis. Sensitivity analysis showed that the probability of duodenal cancer had the strongest effect on the outcome compared with the probability of developing duodenal adenomatosis stage IV or perioperative mortality.

To summarise, the present analysis revealed that surveillance may lead to a moderate gain in life expectancy. Therefore, before starting surveillance of the upper digestive tract, it is important to explain to the patients that the risk of developing duodenal cancer is relatively low and that the only curative treatment for severe duodenal adenomatosis is a major operation with substantial morbidity and mortality (in addition to the morbidity from duodenoscopy). On the basis of this information the patients may be able to decide whether the potential gain in life expectancy outweighs the adverse effects of surveillance and treatment. If the patient prefers to be under surveillance, the screening protocol should start by the age of 30 years. Starting at an earlier age can be considered to offer no clinical benefit, as reports of duodenal cancer before this age are extremely rare. The recommended interval between examinations is one to three years depending on the findings. Ideally, the results should be collected in a uniform manner at a regional or national registry which will permit future evaluation.

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