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Chapter 5

Female fertility after colorectal surgery for familial adenomatous polyposis: A nationwide cross-sectional study

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Female Fertility After Colorectal Surgery for Familial Adenomatous Polyposis
A Nationwide Cross-sectional Study

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Background: Information on postoperative fertility problems in female patients with familial adenomatous polyposis (FAP) is scarce. Previous studies in FAP or colitis patients almost uniformly describe a reduction in fertility after ileal pouch-anal anastomosis, compared with ileorectal anastomosis.

Objective: To describe fertility problems in female FAP patients after colectomy and to investigate the relationship between self-reported fertility problems and the type of operation and other surgery-related factors (e.g., comorbid conditions).

Methods: A questionnaire addressing surgery, fertility problems, and desire to have children was sent to a nationwide sample of FAP patients. Medical data were verified in the FAP-registry of the Netherlands Foundation for the Detection of Hereditary Tumours. Differences between women with and without fertility problems were investigated.

Results: Of 138 patients, 23 (17%) reported current or past fertility problems. The prevalence of fertility problems was similar among those who had undergone ileorectal anastomosis, ileal pouch-anal anastomosis, and proctocolectomy with ileostomy. None of the other surgery-related factors, such as desmoid tumors or cancer, were associated significantly with development of fertility problems. Patients reporting fertility problems were significantly younger at diagnosis of FAP (mean, 20 vs. 27 years; P < 0.05) and at the time of the first surgical procedure (mean, 22 vs. 28 years; P < 0.05).

Conclusions: The risk of developing postoperative fertility problems is not associated significantly with the type of surgery, indication for surgery, complications, or other comorbid conditions. Postoperative fertility problems are more common among women who had their first surgical procedure at a younger age.


In familial adenomatous polyposis (FAP), patients develop multiple (>100) adenomas in the colon, beginning in the second decade of life. A subset of FAP patients also develops extracolonic manifestations including duodenal and gastric adenomas, duodenal cancer, desmoid tumors, osteomas, and rare malignancies. Without treatment, there is a 100% risk of developing colorectal cancer. To prevent cancer, a prophylactic colectomy is performed at a mean age of 26 years. The two main surgical options are a subtotal colectomy with ileorectal anastomosis (IRA) or a proctocolectomy with ileal pouch-anal anastomosis (IPAA). The IRA is a relatively simple procedure with a good functional outcome. However, many patients need a secondary proctectomy later in life as a result of development of polyps or cancer in the remaining rectal mucosa. By performing an IPAA, the need for reoperation because of rectal polyps or cancer is virtually eliminated. However, compared with IRA, the IPAA procedure is a more complicated operation with worse functional outcome. Moreover, sexual problems and reduced fertility rates have been reported after IPAA. These are most often attributed to postoperative anatomic changes in the female pelvis. However, most studies concerning postoperative fertility have focused on patients with inflammatory bowel diseases rather than FAP patients.

The aims of the present study were to describe postoperative fertility problems in female FAP patients and to investigate the association with the type of operation and various surgery-related factors.

METHODS

Data Collection
Participants were drawn from the FAP-registry of the Netherlands Foundation for the Detection of Hereditary Tumours. The results presented here are part of a larger study on the psychosocial effect of FAP.

Invitation letters were sent to a contact person within a family. This was typically a family member (with FAP) who had assisted in drafting the family pedigree at the time of registration, and was often a key figure within the family with regard to counseling issues. The contact person was asked to (1) complete a self-report questionnaire; and (2) assist in inviting other family members by mail to participate in the study. In some families, more than one contact person was recruited because of the large number of family members and branches within the family.

Questionnaires were mailed between October 2005 and January 2007, with a reminder letter sent to all potential participants after 2 weeks. In total, 530 FAP family members participated (64% response rate), among which 341 patients with a genetic or endoscopic established diagnosis of FAP. The questionnaire assessed a range of sociodemographic, clinical, and psychosocial variables. The questionnaire comprised study-specific questions about type and number of surgical procedures, the actual desire for children, and whether fertility problems because of surgery for FAP had been experienced. If the patient reported having experienced fertility problems, she was asked to indicate whether she had had difficulty becoming pregnant, or had failed to become pregnant. There was also the option to describe the nature of the fertility problems.
problems. Self-reported clinical data were confirmed by medical
record audits whenever possible.

The study was approved by the ethics committee of the
Netherlands Cancer Institute and the advisory board of the Nether-
lands Foundation for the Detection of Hereditary Tumors.

Patients

Women with a genetic or endoscopic established diagnosis of
FAP, who had undergone colorectal surgery, and who had returned a
completed questionnaire, were included in the current analysis.

Data Analysis

Continuous variables were compared using the Student’s t
for independent samples. The χ² statistic and Fisher exact test
were used to investigate the influence of categorical variables on
reported fertility problems. A P < 0.05 was considered to be
statistically significant. Data were analyzed using the Statistical
Package for the Social Sciences version 16.0 (SPSS, Chicago, IL).

RESULTS

A total of 341 FAP patients completed the questionnaire, 179
of which were female. Of these women, 138 met the inclusion
criteria, of whom 23 patients (17%) reported current or past fertility
problems. Self-reported problems included difficulty becoming
pregnant (n = 14) and failure to become pregnant (n = 9). In 7
cases, fertility problems could be confirmed through medical record
audit. Problems included tubal occlusion and ovarian dysfunction
because of adhesions.

Table 1 displays the characteristics of the study sample. The
mean age, education level, and marital status of those with and
without fertility problems were comparable. Slightly less than half
of the women who reported having fertility problems had one or
more children, compared with approximately two-thirds of those
without fertility problems. Patients reporting fertility problems were
on average 2 years older at the time of their first pregnancy than
women without fertility problems (29 vs. 27 years, P = 0.28). The
desire for offspring was significantly more often fulfilled in the
group without fertility problems. In both groups, approximately 10%
indicated that they did not currently wish to have (more) children.

As shown in Table 2, the frequency of fertility problems was
not associated significantly with the type of surgery (ie, an IRA,
IPAA, or proctectomy with ileostomy procedure). The data in the
table refer to the last surgical procedure; similar results were
obtained when analyzing "prior surgical procedures" (data not
shown in tabular form). Similarly no significant associations were
observed between the indication for surgery, the occurrence of
desmoid tumors, cancer, or other comorbid conditions and the
prevalence of fertility problems.

Patients reporting fertility problems were significantly
younger at diagnosis of FAP and at the time of the first
surgical procedure (Table 2). The mean age at primary IRA was 27 years,
compared with 24 years at primary IPAA (P = 0.16, data not shown in
tabular form).

DISCUSSION

In this study, we assessed fertility problems in women who
had undergone surgery for FAP. Most remarkable was the compara-
ble numbers of women reporting fertility problems either after
IRA, IPAA, or proctectomy with ileostomy. Also, neither the
indication for surgery, the number of operations and the number of
procedures with complications, nor the occurrence of desmoid
tumors, cancer, or other comorbid conditions were found to be
associated significantly with self-reported fertility problems. How-
ever, women who reported fertility problems after surgery were
substantially younger when diagnosed with FAP and at the time of
first colectomy than women who did not experience fertility
problems. The women with fertility problems had their first child at a
later age, suggesting that early surgery has a negative influence on
fertility.

Previous reports on the effect of surgical procedure on fertility
almost uniformly describe a reduction in fertility after IPAA.8,10,16–20
However, most of these studies were on ulcerative colitis patients. Only two studies described female fertility after surgery for FAP.8,21 The study of Johansen et al found that 10% of the women had an unfilled desire to become pregnant, corre-
spending with the estimated population infertility rate.21

Olsen et al22 compared fecundity, defined as the probability of
becoming pregnant per month by unprotected intercourse, in 162
women who had undergone IRA or IPAA and a reference population
including 914 women from the general population. Patients after
IRA had a greater fecundity than the reference population, but
fecundity after IPAA was severely reduced. Contrary to our study, in
which the ages at IPAA and IRA did not differ significantly, in the
study of Olsen et al, patients who underwent IPAA were signifi-
cantly older. This may explain, in part, the decreased fecundity rates
in the study of Olsen et al among those who had undergone IPAA.
A further difference from our study was the way of assessing
reproductive function.

<table>
<thead>
<tr>
<th>TABLE 1. Sociodemographic Data, Number of Children and Desire to Have Children of Patients With and Without Fertility Problems due to Colorectal Surgery (n = 138)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With Fertility Problems (n = 23)</strong></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
</tr>
<tr>
<td>Partner</td>
</tr>
<tr>
<td>Single</td>
</tr>
<tr>
<td>Divorced</td>
</tr>
<tr>
<td>Widow</td>
</tr>
<tr>
<td><strong>Children</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Age at first pregnancy</strong></td>
</tr>
<tr>
<td>Mean (range)</td>
</tr>
<tr>
<td><strong>Desire to have (more) children</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Reason</strong></td>
</tr>
<tr>
<td>Desire fulfilled</td>
</tr>
<tr>
<td>I don’t want children</td>
</tr>
<tr>
<td>Don’t know/no partner</td>
</tr>
<tr>
<td><strong>Level of education</strong></td>
</tr>
<tr>
<td>Primary school</td>
</tr>
<tr>
<td>High school</td>
</tr>
<tr>
<td>College/university</td>
</tr>
<tr>
<td><strong>Current age</strong></td>
</tr>
<tr>
<td>Mean (range)</td>
</tr>
</tbody>
</table>

*Significant at 0.05 level (2-tailed).
TABLE 2. The Frequency of Fertility Problems in Relation to Surgery and Comorbidity and Mean Ages at Diagnosis of FAP and at Primary and Secondary Surgery (n = 138)

<table>
<thead>
<tr>
<th>Type of last surgery</th>
<th>With Fertility Problems (n = 33)</th>
<th>Without Fertility Problems (n = 115)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRA</td>
<td>9 (30)</td>
<td>49 (42)</td>
<td>0.56</td>
</tr>
<tr>
<td>IPAA</td>
<td>9 (30)</td>
<td>51 (44)</td>
<td></td>
</tr>
<tr>
<td>Proctocolectomy and ileostomy</td>
<td>5 (22)</td>
<td>15 (13)</td>
<td></td>
</tr>
<tr>
<td>Indication first operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>22 (96)</td>
<td>110 (96)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cancer</td>
<td>1 (4)</td>
<td>5 (4)</td>
<td></td>
</tr>
<tr>
<td>No. operations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16 (70)</td>
<td>90 (78)</td>
<td>0.37</td>
</tr>
<tr>
<td>&gt;1</td>
<td>7 (30)</td>
<td>25 (22)</td>
<td></td>
</tr>
<tr>
<td>Complications (adhesions, bleeding, abscess)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (52)</td>
<td>44 (38)</td>
<td>0.22</td>
</tr>
<tr>
<td>No</td>
<td>11 (48)</td>
<td>71 (62)</td>
<td></td>
</tr>
<tr>
<td>Desmoid tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (17)</td>
<td>14 (12)</td>
<td>0.50</td>
</tr>
<tr>
<td>No</td>
<td>19 (83)</td>
<td>101 (88)</td>
<td></td>
</tr>
<tr>
<td>Cancer (colorectal, thyroid, skin, cervix, non-Hodgkin lymphomas)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (13)</td>
<td>13 (11)</td>
<td>0.73</td>
</tr>
<tr>
<td>No</td>
<td>20 (87)</td>
<td>102 (89)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity (Cardiovascular or pulmonary diseases, cerebrovascular accidents, diabetes, osteoarthritis, kidney failure, malignant tumors, psychological complaints)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (52)</td>
<td>62 (54)</td>
<td>0.81</td>
</tr>
<tr>
<td>No</td>
<td>11 (48)</td>
<td>53 (46)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean (Range)</th>
<th>n</th>
<th>Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis of FAP</td>
<td>23</td>
<td>20 (6–36)</td>
<td>115</td>
<td>27 (9–58)</td>
</tr>
<tr>
<td>Age at first operation</td>
<td>23</td>
<td>22 (10–36)</td>
<td>114</td>
<td>28 (10–59)</td>
</tr>
<tr>
<td>Age at second operation</td>
<td>7</td>
<td>36 (26–54)</td>
<td>18</td>
<td>39 (17–59)</td>
</tr>
</tbody>
</table>

Pearson χ²; Fisher exact test was performed for Desmoid tumour and Cancer, because of small numbers. *Significant at 0.01 level (2-tailed).

IRA indicates ileorectal anastomosis; IPAA, ileal pouch-anal anastomosis.

A major strength of our study is the large number of participating FAP patients and the availability of detailed information about surgery, complications, and comorbidity. Furthermore, we were able to verify part of the self-reported problems with medical data.

A potential weakness of the study is the lack of detailed information on the “time to pregnancy,” something that is difficult to assess accurately in a retrospective study.²² Also, no information on fertility problems before surgery was available.

Reduced fertility after colorectal surgery is most often attributed to postoperative anatomic changes in the female pelvis.¹¹,¹²,¹³ As IPAA is a more complicated procedure than IRA, more tissue damage and postoperative adhesions would be expected after IPAA and multiple operations.¹⁴ However, we found a similar rate of fertility problems after IRA and IPAA. The higher incidence of fertility problems after IPAA reported in earlier studies may be explained, at least in part, by the inclusion of ulcerative colitis patients.

We found that women with fertility problems were significantly younger at the time of the first surgical procedure, compared with women without fertility problems. Women with fertility problems who were able to get children had their first child on average 7 years after the first surgical procedure. Patients with children who reported no fertility problems had their first child on average 1 year before their first operation. These findings suggest that a colectomy early in life may lead to subfertility. However, patients may have postponed pregnancy for other reasons. Possibly, women who reported no fertility problems and had their first child before surgery did not perceive themselves as having fertility problems because their family was already complete. Because of the cross-sectional study design and because part of our population has no children at all we are unable to correct for this variable.
In our study, 1 of 6 female FAP patients indicated having had reduced fertility because of surgery. In the general Dutch population, 1 of 10 of the couples have subfertility complaints at least once during their lifetime. However, these latter figures include both male and female fertility problems, making comparison with our results difficult.

In our study, the risk of developing fertility problems could not be attributed to the IPAA procedure exclusively, as patients after IRA reported the same frequency of fertility problems as those who had undergone other surgical procedures. For primary surgery, an IRA procedure is preferred because of the lower complication risk. The IPAA procedure should be considered the primary surgery of choice for polyposis patients with extensive rectal involvement. Based on the present study, concerns about fertility problems after IPAA may be of less importance than previously thought.

Further studies are needed to investigate the effect of less invasive surgical (laparoscopic) methods and to clarify the nature of fertility problems in FAP patients in more detail. The best way to evaluate subfertility would be a prospective analysis of the “time to pregnancy.”

In conclusion, for female FAP patients, no association was found between fertility problems and type of surgery, other surgical-related factors, desmoid tumors, cancer, and other comorbidity. Women reporting postoperative fertility problems had their first surgical procedure earlier in life than women not reporting such problems. Female FAP patients should be well informed about the pros and cons of both procedures and the risk of reduced fertility later in life after both IRA and IPAA.

ACKNOWLEDGMENTS

The authors thank all of the individuals from the FAP families who participated in this study.

REFERENCES
