Functional outcome and quality of life after rectal resection
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Chapter 7

WHAT IS THE BENEFIT OF PREOPERATIVE SPERM PRESERVATION FOR PATIENTS, WHO UNDERGO RESTORATIVE PROCTOCOLECTOMY FOR BENIGN DISEASES?


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Abstract

**Background/Aims:** In patients with benign colorectal diseases undergoing a restorative proctocolectomy with an ileal pouch-anal anastomosis (IPAA), semen cryopreservation (SC) seems rational to warrant the possibility of procreation in case surgery would have lead to sexual disorders or impotence. The aim of this study was to determine the pre- and post-operative semen quality in patients undergoing IPAA, and the incidence of surgery induced sexual dysfunction in order to evaluate the economic efficiency of SC, as compared to alternatives like microsurgical epididymal sperm aspiration (MESA).

**Methods:** Pre and post-operative semen analyses were offered to 97 IPAA patients with benign colorectal diseases since 1989. The direct costs of the SC program were determined and compared with those of alternatives.

**Results:** In 34 out of 40 consecutive IPAA patients who made use of pre-operative semen preservation, normal sperm concentrations, motility and morphology were found. Mean semen characteristics of all 23 patients who returned for postoperative analysis were not different from preoperative values, but for total number of spermatozoa. Two patients developed temporarily retrograde ejaculation postoperatively. None of the preserved semen samples were used, thus SC benefited none of these patients. The total costs of SC are between 2.2 and 5 times higher than the costs for one MESA procedure.

**Conclusion:** Preoperative SC in patients undergoing IPAA because of benign colorectal diseases is feasible. However, most likely due to improved surgical techniques and the increasing number of effective alternatives, preoperative SC in IPAA patients is no longer cost-effective.
Introduction

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) has gained wide acceptance in the surgical treatment of patients with chronic ulcerative colitis (UC)\textsuperscript{1} and familial adenomatous polyposis (FAP).\textsuperscript{2} The procedure enables eradication of colorectal disease by removing all colorectal mucosa at risk and restores intestinal bowel continuity with preservation of close to normal function. Moreover, by avoiding a permanent ileostomy, IPAA improves the patient’s quality of life as compared to those who underwent a conventional total proctocolectomy with ileostomy.\textsuperscript{3,4} The procedure however, is not without problems. Proctocolectomy in male patients carries some risk of nerve damage that may lead to sexual dysfunction, such as erectile failure and retrograde ejaculation. In addition, UC patients’ semen quality can be impaired due to the side effects of anti-inflammatory medication. Anticipating these possible disadvantages, pre-operative semen cryopreservation has been offered since 1989 to all males undergoing an IPAA to warrant eventual procreation. Since the reported incidence of impotence is low after this procedure\textsuperscript{1} and alternatives for semen preservation such as microsurgical epididymal sperm aspiration (MESA) have become available, it is disputable whether semen banking in patients undergoing an IPAA is rational.

The aim of this study is to estimate the feasibility and effectiveness of pre-operative semen-preservation in patients undergoing IPAA. Therefore the patients’ pre- and post-operative semen quality was determined as well as the incidence of post-operative temporary or permanent sexual dysfunction.
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Methods

Patients
Between March 1985 and March 1998, 97 male patients at the Academic Medical Center in Amsterdam underwent a restorative proctocolectomy with an IPAA. Semen cryopreservation was offered to all of these men prior to the operation. Fifty-seven out of these 97 male patients decided not to make use of the possibility of pre-operative cryopreservation, because of a complete family, preexistent infertility, previous vasectomy or other personal reasons. Thus forty patients with a mean age of 31 years (range 22 - 43 years) enrolled in a preoperative cryopreservation program. The clinical and histology data were obtained by retrospective review of the charts. Analysis of the semen was done according to regulations as stated by the WHO. At least four months after the operation, all patients were requested to deliver a second semen sample for analysis. If the quality of the semen sample was within the normal limits as defined by the WHO standards, the patients were asked whether they agreed that the pre-operative sample was destroyed.

Assessment and calculation of the costs
The direct costs of the cryopreservation program were determined by the tariffs set by the Dutch Central Organ for Healthcare Tariffs (COTG), based upon the charges for preoperative outpatient visits, sperm analysis pre- and post-operatively, cryopreservation of 3 sperm samples, administration costs, follow-up, and if asked for, costs of specimen destruction. These costs were compared to those reported previously for MESA. The costs of the cryopreservation program were calculated in Euro’s. The official exchange rate at February 4th 1999 was 1$ = 0.88€. A number to treat approach was used to present the trade-off between whole-group preservation versus the maximum number of beneficiaries where the MESA procedure could be an alternative. Only the costs to obtain a viable semen sample are taken into account, although there will be considerable more costs in an attempt to achieve a pregnancy by assisted reproduction procedures.

Statistical analysis
All results were expressed as means (SD). Paired Student’s t-tests were used for pre- and post-operative comparisons, p values < 0.05 were considered statistically significant.
Results

Clinical outcome
The semen of forty IPAA patients was cryopreserved preoperatively during the study period. Details on the surgical technique of a restorative proctocolectomy with an IPAA procedure have been reported in previous communications. In brief, after abdominal colectomy, the rectum is dorsally mobilized by dissection through the avascular plane. At the ventral side, the rectum is mobilized dorsal of the Denonvillier’s fascia. The lateral structures are divided close to the rectal wall. The transection of the rectum is accomplished by a transverse stapler at the ano-rectal junction, as established by endoanal inspection. Finally a J-pouch is anastomosed with the proximal anal canal by means of a circular stapling technique. Thirty-five patients were operated because of therapy resistant UC and five patients because of other reasons (Table 1). The diagnosis was adjusted in eight of the 35 UC patients after microscopic examination. Six patients were classified as suffering from indeterminate type colitis (IC) and in two patients were judged to have Crohn’s disease. Two of the 40 patients suffered temporary sexual disorders post-operatively, both patients developed retrograde ejaculation, but recovered completely. In 48% of all patients a temporary ileostomy was constructed, which was taken down within a median period of 4 months (range 3-21 months).

Table 1:

<table>
<thead>
<tr>
<th>Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Mean age years (SD)</td>
</tr>
<tr>
<td>Mean follow-up years (SD)</td>
</tr>
<tr>
<td>Diagnose</td>
</tr>
<tr>
<td>UC</td>
</tr>
<tr>
<td>IC</td>
</tr>
<tr>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>FAP</td>
</tr>
<tr>
<td>Hirschsprung’s</td>
</tr>
<tr>
<td>disease</td>
</tr>
<tr>
<td>Preoperative medication</td>
</tr>
<tr>
<td>sulphasalazine</td>
</tr>
<tr>
<td>mesalazine</td>
</tr>
<tr>
<td>prednison</td>
</tr>
<tr>
<td>azathioprine</td>
</tr>
<tr>
<td>Diverting ileostomy</td>
</tr>
<tr>
<td>Pouch removed</td>
</tr>
</tbody>
</table>

UC = ulcerative colitis; IC = indeterminate colitis; FAP = familial adenomatous polyposis.
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Post operative complications resulting in a relaparotomy occurred in eight patients, four patients because of persisting intestinal obstruction and one because of anastomotic leakage requiring a temporary ileostomy. In three patients the pouch had to be excised and a permanent ileostomy was constructed. This was necessary in two patients because of recurrent anastomotic fistula. Both patients’ diagnosis were postoperatively changed from UC to IC. The third patient’s pouch was removed because of therapy-resistant pouch dysfunction. Twenty-seven of the 35 inflammatory bowel disease (IBD) patients, used preoperatively anti-inflammatory medication such as sulphasalazine, mesalazine, prednison, azathioprine, or a combination of these drugs (Table 1). This medication was discontinued postoperatively in all these patients.

Semen analysis and fertility
Twenty-three of the 40 patients with preoperatively cryopreserved semen who underwent IPAA, returned to the semen bank for postoperative semen analysis. The seventeen patients not returning for analysis did so for various reasons. Two of them fathered a child postoperatively and asked for destruction of their preoperative semen specimens. Another eight experienced no sexual dysfunction and did not want to come for a second analysis. One patient did not return because pre-treatment semen analysis showed poor semen parameters which did not allow cryopreservation. The other six patients did not return for personal reasons other than sexually related.

The mean sperm concentration in the preoperative group was 71 (range 1-200) million spermatozoa per ml and the mean forward progression percentage was 38% (range 0-64%). Eight patients fathered one or more children pre-operatively. Six patients out of the whole group had preoperative sperm concentrations, sperm motility and morphology percentages below the lower limit as set by the WHO standards. Five of them were UC patients and one had FAP. No clear relation between poor semen quality and use of anti-inflammatory drugs could be demonstrated, since only three of these five UC patients used anti-inflammatory medication. Two out of these three who returned for postoperative analysis, regained normal semen quality, after the medication had been discontinued. One of them fathered a child. There were no differences in preoperative semen quality of IBD patients who used either one anti-inflammatory drug, or a combination of various drugs as compared to IBD patients without this type of medication.

Mean semen characteristics of 23 patients who underwent pre- and postoperative semen analysis showed no differences between pre- and postoperative values, but for total sperm number, which was significantly larger before the operation (Table 2). Seven of the 40 patients fathered a child postoperatively. IBD patients
who used anti-inflammatory medication showed no significant improvement in semen quality postoperatively after administration of these drugs had been stopped.

<table>
<thead>
<tr>
<th></th>
<th>Normal limits</th>
<th>Pre-operative values</th>
<th>Post-operative values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume ml</td>
<td>≥2.0</td>
<td>3.0 (1.6)</td>
<td>2.8 (1.7)</td>
</tr>
<tr>
<td>pH</td>
<td>7.2 - 7.8</td>
<td>7.6 (0.3)</td>
<td>7.5 (0.2)</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>≥20 10⁶ spermatozoa / ml</td>
<td>82 (58)</td>
<td>80 (101)</td>
</tr>
<tr>
<td>Total perm count</td>
<td>≥40 10⁶ spermatozoa / ml</td>
<td>232 (226)</td>
<td>160 * (151)</td>
</tr>
<tr>
<td>Sperm motility</td>
<td>≥50 forward progression %</td>
<td>41 (16)</td>
<td>37 (15)</td>
</tr>
<tr>
<td></td>
<td>≤50 slow progression %</td>
<td>7 (7)</td>
<td>9 (8)</td>
</tr>
<tr>
<td></td>
<td>≤50 immotile %</td>
<td>51 (12)</td>
<td>54 (11)</td>
</tr>
<tr>
<td>Normal morphology %</td>
<td>≥40</td>
<td>47 (20)</td>
<td>41 (15)</td>
</tr>
<tr>
<td>'Round' cells</td>
<td>24 (36)</td>
<td>8 (5)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Semen Analysis

Semen analysis preoperative vs. postoperative values n = 23. * p < 0.05, paired t test. Data are expressed as means with SD in brackets.

Twenty out of 23 patients (87%) whose semen had been preserved pre- and postoperatively, achieved sperm counts of more than 20 x 10⁶ spermatozoa / ml. The remaining three patients had a mean sperm concentration of 7.3 x 10⁶ spermatozoa / ml with 21% progressive motility. None of the preoperative cryopreserved semen specimens were used in an in-vitro fertilization procedure.

Cost comparison

The complete cryopreservation program costs consist of $43 for an initial semen analysis and analysis following freezing and thawing. The preparing and freezing costs of three semen specimens are $240 and long-term storage costs are $40 per year. To the aforementioned costs, the administration costs, follow-up, and if asked for, costs of specimen destruction are added. According to these data the total costs of pre-operative cryopreservation stored for two years were $391. The overall costs of the cryopreservation program for these 40 patients were $15640. The most recent reported costs for MESA are respectively $3123 and $7106 per patient⁶,⁷. The latter amount was based upon physician and hospital charges; preoperative history and physical examination; operation and recovery room charges as the first amount was based upon the median costs that were made for all patients who underwent MESA. The total costs for the cryopreservation program benefited none of the patients in this study, and are between 2.2 and 5 times higher than the charge per sperm specimen obtained through MESA.
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Discussion

Adult male patients with benign colorectal diseases who have to undergo IPAA face a potential risk to develop sexual dysfunction postoperatively. Pre-operative cryopreservation of semen therefore seems to be a rational preventive strategy. Patients are offered the chance to have, or complete their own family regardless of the eventual impact of surgery on sexual functioning or semen quality. There is little information in the literature regarding the practicality, availability, logistics and costs of autologous semen banking in these patients. The best treatment option at present for UC or FAP patients is an IPAA. This procedure eradicates nearly all-diseased colon mucosa, restores the intestinal continuity and has good long-term functional results. There is a potential risk for surgical nerve damage leading to sexual dysfunction. Sexual dysfunction in males summarizes conditions such as erectile dysfunction or loss of the ability to ejaculate which can either be permanent, complete or partial. The former is induced by surgically damaging the parasympathic splanchic nerves and the latter due to damaging the sympathetic hypogastric plexus. Sexual dysfunction and impotence occur after IPAA, between 3 and 6% and 1 and 4% respectively. The incidence of these sexual complication rate is, however, likely to decrease since it has been reported that the incidence of surgical complications is declining due to increasing experience with, and standardization of the IPAA procedure. Besides the possible impact of surgery on fertility, it should be kept in mind that semen quality can be impaired in patients with inflammatory bowel disease due to the side effects of anti-inflammatory medication. Several studies have shown that sulfasalazine or azathioprine can have adverse effects on semen quality, returning to normal after these drugs are discontinued. This study showed that 85% of all males regardless of their medication, who have to undergo IPAA for benign colorectal diseases, have normal semen specimens that could be cryopreserved preoperatively. Only six patients (15%) had oligozoospermia preoperatively according to the WHO standards. No clear relationship with possible side-effects of anti-inflammatory medication could be shown. Patients with oligozoospermia are not necessarily infertile, for pregnancies have been reported after in vitro fertilization (IVF) or zygote intrafallopian transfer or ultimately intracytoplasmic sperm injection (ICSI) with semen specimens concentrations less than $1 \times 10^6$ spermatozoa / ml. Preoperative semen specimen storage could therefore be offered to almost every patient. Two of the study patients (5%) experienced impairment of their sexual functioning postoperatively. Both patients temporarily developed retrograde ejaculation. Both patients have requested to destroy their preoperative semen
samples since they had no wish to expand their families. Moreover, in case of permanent retrograde ejaculation it is possible to obtain viable semen out of a sample of urine for intra-uterine insemination (IUI) or IVF. The total cost for semen preservation for all 40 patients in this study was $15640, but none has actually benefited from these efforts until now. If we assume a maximum of 1 beneficiary of this strategy, then these costs are between 2.2 and 5 times higher as compared to the reported costs for a single MESA procedure, excluding the costs for the assisted reproduction procedures. In addition to this, costs of alternatives of preoperative semen banking could be even less if percutaneous alternatives to MESA, such as biopsy or needle aspiration from the testis become more available. In conclusion, patients with benign colorectal diseases who have to undergo an IPAA can provide semen samples with sufficient quality for preoperative cryopreservation. However, in view of the declining surgical risk for postoperative sexual dysfunction and the increasing number of effective less costly alternatives, preoperative semen banking does not seem to be optional anymore in this group of patients.

References

SEMEN PRESERVATION NEEDED BEFORE IPAA?