Technical Issues and Early Outcomes of Restorative Proctocolectomy for Familial Adenomatous Polyposis and Ulcerative Colitis: The Largest Romanian Single-Team Experience

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Rezumat

Elemente de tehnică și rezultatele postoperatorii imediate după proctocolectomia totală restaurativă pentru polipoză adenomatoasă familială și rectocolită ulcero-hemoragică: experiența unei singure echipe chirurgicale

Introducere: Proctocolectomia totală restaurativă este un procedeu chirurgical complex folosit în cazul pacienților diagnosticați cu polipoză adenomatoasă familială și rectocolită ulcero-hemoragică. Studiul de față își propune să analizeze elemente de tehnică chirurgicală, precum și rezultatele postoperatorii imediate după proctocolectomia totală restaurativă, pe baza experienței acumulate de către o singură echipă chirurgicală.

Pacienți și Metodă: Datele tuturor pacienților cu proctocolectomia totală restaurativă efectuate de către o singură echipă chirurgicală în perioada 1991 – 2018 au fost analizate retrospectiv, având în vedere existența unei baze de date cu intervenții chirurgicale introduse prospectiv.

Rezultate: Au fost incluși în studiu un număr de 77 de pacienți cu proctocolectomie totală restaurativă, dintre care 70,1% au avut diagnosticul de polipoză adenomatoasă familială. Numărul mediu anual de proctocolectomii totale restaurative a fost de 3,3 pentru echipa chirurgicală inclusă în studiu, și 4,3 la nivel instituțional. Un rezervor de tip J a fost realizat la 93,5% dintre pacienți; în
Introduction

Restorative proctocolectomy (RPC) is a complex colorectal surgical procedure that is mainly used to treat patients with ulcerative colitis (UC) and familial adenomatous polyposis (FAP) (1). FAP is an inherited disease that is classically characterized by the development of hundreds to thousands of adenomas in the rectum and colon during the second decade of life (2). A less aggressive variant of FAP is so-called attenuated FAP, where the rectum is
frequently spared (2).

Although FAP is responsible for less than 1% of the colorectal malignancies, however, untreated individuals with FAP carry a 100% risk of colorectal cancer by the ages of 40-50 years (2). Thus, for patients with FAP, the single way to prevent colorectal cancer is surgery (3).

The surgical options to treat FAP are total colectomy with ileo-rectal anastomosis (for attenuated FAP) and RPC (for classical FAP) (3). Nowadays, it is widely accepted that RPC is the procedure of choice to treat patients with FAP (2,3).

UC is a chronic inflammatory condition characterized by continuous mucosal inflammation of the colon and rectum (4). Nowadays, surgery is required in a limited number of patients with UC, either in an elective or in an emergency setting (5,6). In patients with UC and indication for surgery, RPC is widely considered the gold standard surgical procedure, although total colectomy with ileo-rectal anastomosis can be used for some particular cases (4,7,8).

Emergent colectomy is indicated in few cases of severe acute UC, not responding to medical therapy or when complications such as severe bleeding, toxic megacolon or perforation occur (8). In these particular situations, the timing of colectomy is of utmost importance to reduce postoperative complications rates (8).

Elective RPC is indicated in chronic refractory UC, presence of high-grade dysplasia or colorectal malignancies (8). The risk of colorectal cancer in UC is increased compared with the general population, and it is estimated to be around 18% after 30 years of UC duration (9).

It is worth mentioning that the decision to perform surgery in a patient with UC should be made in a multidisciplinary team including the gastroenterologist and colorectal surgeon (8).

The present study aims to assess the technical issues and early outcomes of RPC for FAP and UC, in a relatively large single-team series of patients.

Patients and Methods

The data of all patients with RPC performed between 1991 and 2018 by a single surgical team (leading operator or supervisor Mihnea Ionescu) were retrospectively assessed from a prospectively maintained electronic database established in Fundeni Clinical Institute. Our technique of RPC was previously described elsewhere (1).

The analyzed data included pre-operative (demographics, indications of surgery, co-morbidities) and intraoperative parameters (operative time, blood loss, details of technique), as well as the early postoperative outcomes. The early morbidity and mortality were defined as in-hospital, after ileal pouch-anal surgery. The Dindo classification and grading of post-operative complications were used (10). A complication grade 3 or 4 was considered a severe complication.

Statistical Analysis

Data are expressed as number (percentage) for the categorical variables and as mean (± standard deviation) for the continuous variables. The comparisons between the groups were made using the Mann-Whitney test (for the continuous variables) and the Fisher’s exact test, two-tailed (for the categorical variables). P values less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS (Statistical Packages for Social Sciences) version 20.0 software (SPSS Inc., Chicago, IL).

Results

Demographics and Pre-operative Parameters

Between 1991 and 2018, 99 RPC were performed in Fundeni Clinical Institute, and 77 patients (78.8%) (the study group) were operated by the Mihnea Ionescu surgical team (Fig. 1). Thus, the average number of RPC per year in Fundeni Clinical Institute was 4.3,
while for Mihnea Ionescu team it was 3.3 RPC/ year.

In the study group of patients, 39 patients (50.6%) were women, and the mean age was 32 ± 12 years.

The indications for RPC were FAP in 54 patients (70.1%) and UC in 23 patients (29.9%) (Fig. 2). The most substantial part of RPC was performed as elective surgery (74 patients – 96.1%), while three patients (3.9%, all with UC) were operated in an emergency setting.

The patients in the FAP group were significantly younger, compared with those in the UC group (30 ± 12 vs. 37 ± 12 years, p = 0.025).

The presence of colo-rectal malignancies at the time of ileal pouch-anal surgery was observed in 17 patients (22.1%). The presence of colo-rectal malignancies was significantly higher in the FAP group of patients, compared with the UC group (29.6% vs. 4.3%, p = 0.015). The malignancies were observed in the left colon in 9 patients (11.7%), right colon in 5 patients (6.5%), upper and mid rectum in 5 patients (6.5%), transverse colon in 3 patients (3.9%) and recto-sigmoid in 2 patients (2.6%). Seven patients (9.1%) presented with multiple locations of colo-rectal malignancies.

The overall rate of colo-rectal malignancies (including those before ileal pouch-anal surgery) was 27.3% (21 patients). The presence of overall colo-rectal malignancies was significantly higher in the FAP group of patients, compared with the UC group (35.2% vs. 8.7%, p = 0.023).

Previous colectomies were performed in 15 patients (19.5%). The percentage of previous colectomies was significantly higher in the UC group of patients, compared with the FAP group (39.1% vs. 11.1%, p = 0.009). Thus, in the group of patients with FAP, three patients (out of 54 patients, 5.6%) have had previous segmental colectomies for malignancies, while three patients (5.6%) have had RPC for rectal
stump adenomas development after previous total colectomy with ileo-rectal anastomosis. In the UC group of patients, eight patients (out of 23 patients, 34.8%) have had previous total colectomies either in an elective (3 patients, 13%) or in an emergent setting (5 patients, 21.7%). In two patients (8.7%) with elective surgery, an ileo-rectal anastomosis was performed. One patient (4.3%) in the UC group of patient underwent previous segmental colectomy for perforation.

Co-morbidities were present in only five patients (6.5%).

**Intraoperative Data and Technical Issues**

A J pouch was performed in 72 patients (93.5%), while the S pouch was performed in only five patients (6.5%) (Fig. 3). A hand-sewn reservoir was made in 59 patients (76.6%), while the linear staplers were used in 18 patients (23.4%) (Fig. 4).

A hand-sewn ileal pouch-anal anastomosis was performed in 63 patients (81.8%), while a double-stapled anastomosis was used in 14 patients (18.2%) (Fig. 5, 6). The use of double-stapled ileal pouch-anal anastomosis was significantly higher in the UC group of patients, compared with the FAP group (52.2% vs. 1.9%, p < 0.001).

A diverting ileostomy was performed for the most substantial part of patients in the present series (71 patients – 92.2%).

Mucosectomy was performed in 65 patients (84.4%) (Fig. 7). All the patients in the FAP group of patients underwent mucosectomy, while in the UC group, 11 patients (47.8%) have had mucosectomy. Statistically significant differences were observed between the groups regarding the use of mucosectomy (p < 0.001).

Fourteen patients (18.2%) required the use of lengthening techniques of the mesentery to allow a tension-free ileal pouch-anal anastomosis (Fig. 8). The percentage of patients requiring the use of lengthening techniques was significantly higher in the group of FAP patients, compared with the UC group (25.9% vs. 0%, p = 0.007).

Eight patients (10.4%) have had associated surgical procedures at the time of ileal pouch-anal surgery.

The mean operative time was 238 ± 51 min, with no significant differences between the groups.
Figure 5. The type of ileal pouch-anal anastomosis in 77 patients with RPC

Figure 6. Intraoperative aspects of the ileal pouch-anal double-stapled anastomosis: (A) J pouch with anvil inside; (B) double-stapled ileal pouch-anal anastomosis

Figure 7. Intraoperative aspects after mucosectomy

Figure 8. Intraoperative aspects of lengthening techniques to allow a tension-free ileal pouch-anal anastomosis: (a) preservation of the ileo-colic vessels (arrow); (b) prior clamping with bulldog clamp to assess the viability of the distal ileum before the mesenteric vascular division
FAP and UC groups of patients (240 ± 54 vs. 234 ± 46 min, p = 0.915).

The mean estimated blood loss was 249 ± 56 ml, with no significant differences between the FAP and UC groups of patients (241 ± 61 vs. 250 ± 40 ml p = 0.861).

**Early Postoperative Outcomes**

At least one complication was observed in 28 patients (36.4%) with RPC in an early setting, as shown in Table 1. The Dindo grading of complications is shown in Fig. 9. Thus, severe complications were observed in 10 patients (13%).

No significant differences between the FAP and UC groups of patients were observed for the overall and severe complication rates (40.7% vs. 21.7%, p = 0.126 and 14.8% vs. 8.7%, p = 0.714).

Nine patients (11.5%) required re-laparotomy for postoperative complications (Table 2), with no significant differences between the FAP and UC groups of patients (13% vs. 8.7%, p = 1).

The mean hospital stay was 13 ± 6 days, with no significant differences between the FAP and UC groups of patients (13 ± 7 vs. 13 ± 5 days, p = 0.652).

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients (%)</th>
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<tbody>
<tr>
<td>Pouch-related septic complications</td>
<td>14 patients (18.2%)</td>
</tr>
<tr>
<td>Pouch or ileo-anal anastomosis leak</td>
<td>5 patients (6.5%)</td>
</tr>
<tr>
<td>Pelvic abscess</td>
<td>4 patients (5.2%)</td>
</tr>
<tr>
<td>Acute peritonitis (± pouch necrosis)</td>
<td>3 patients (3.9%)/ 2 patients (2.6%)</td>
</tr>
<tr>
<td>Pouch-vaginal fistula</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Hemorrhagic complications</td>
<td>5 patients (6.5%)</td>
</tr>
<tr>
<td>Pelvic hematoma</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Hemoperitoneum</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Retroperitoneal hematoma</td>
<td>1 patient (1.3%)</td>
</tr>
<tr>
<td>Pouch hemorrhage</td>
<td>1 patient (1.3%)</td>
</tr>
<tr>
<td>Other complications</td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td>7 patients (9.1%)</td>
</tr>
<tr>
<td>Small-bowel obstruction</td>
<td>5 patients (6.5%)</td>
</tr>
<tr>
<td>Central venous catheter infection</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Urinary infection</td>
<td>1 patient (1.3%)</td>
</tr>
<tr>
<td>Pulmonary embolism and death</td>
<td>1 patient (1.3%)</td>
</tr>
</tbody>
</table>

Figure 9. Dindo grading of complications in 77 patients with RPC
Discussion

Worldwide, the first series of RPC was published in 1978 at St. Mark’s Hospital in London (UK) and included patients with UC (11). The first RPC in Romania was performed in 1991 in Fundeni Clinical Institute in a patient with malignant FAP. The particular outcomes of the first Romanian patient with RPC were previously presented elsewhere (12).

It is worth mentioning the merit of Mihnea Ionescu to introduce and furthermore developed this surgical technique in Romania. Noteworthy, he had trained several other surgeons to perform this complex surgical procedure in Fundeni Clinical Institute and a few other surgical centers. Nevertheless, the early experiences of Fundeni Clinical Institute with RPC were previously described in several papers (7,13,14).

To the best of our knowledge, this is the most extensive published series of Romanian patients with RPC. However, this procedure is also performed in other Romanian surgical centers, but the published data are scarce (15).

The present series of RPC has some particularities compared with the Western ones. Thus, in the present series, the most common indication for RPC was FAP (70.1% of patients), while in the Western series, UC represents the main indication (68 – 93%) (16-20). This difference can be explained at least in part by the lower incidence of UC in Romania, compared with the Western countries (21,22). Furthermore, it appears that the Romanian UC patients have low rates of severe, extensive or complicated disease and a small proportion of those patients need surgery (21). In the future, an increased incidence of UC in Romania is expected because of the adoption of a Western style of food and living.

The presence of colo-rectal malignancies is not a contraindication for a RPC except for the low rectal location when an oncologically safe sphincter-saving operation is not possible (1).

Table 2. Indications of re-laparotomy for postoperative complications in 77 patients with RPC

<table>
<thead>
<tr>
<th>Indication of surgery</th>
<th>Surgical procedure</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute peritonitis (± pouch necrosis)</td>
<td>Ileal pouch excision</td>
<td>3 patients (3.9%)</td>
</tr>
<tr>
<td>Hemoperitoneum</td>
<td>Bleeding control</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Pelvic abscess and small-bowel obstruction</td>
<td>Drainage and viscerolisis</td>
<td>2 patients (2.6%)</td>
</tr>
<tr>
<td>Ileal pouch-vaginal fistula</td>
<td>Ileostomy</td>
<td>2 patients (2.6%)</td>
</tr>
</tbody>
</table>

Figure 10. Intraoperative aspects with preservation of the autonomic pelvic nerves during RPC: (A) preservation of the left hypogastric nerve (arrow); (B) careful dissection of the rectum posterior to the Denovillier’s fascia (arrow)
However, when the malignancies are present, an oncological resection should be performed depending on the site of the tumor. Nevertheless, preservation of the autonomic pelvic nerves during RPC is of utmost importance in both malignant and non-malignant patients with FAP or UC, to maximize the functional outcomes (Fig. 10), but the anatomic variability and the inability to visualize the small fibers of the inferior hypogastric plexus may explain the occurrence of some postoperative visceral and sexual dysfunctions despite of careful dissection and adequate surgical technique (23). In the current series, colorectal malignancies at the time of ileal pouch-anal surgery were observed in 22.1% of patients, with a significantly higher incidence in the FAP group of patients, compared with the UC group (29.6% vs. 4.3%, p = 0.015).

A two-stage RPC (i.e., initially recto colectomy with ileal-pouch anastomosis and diverting ileostomy; followed in a second stage by ileostomy closure) is widely recommended for FAP and elective patients with UC (1). The current European Crohn's and Colitis guidelines for UC recommend a three-stage RPC (i.e., initially subtotal colectomy with an ileostomy, followed by ileal-pouch anastomosis and diverting ileostomy in a second stage, and closure of ileostomy as a third stage) in patients with acute severe colitis taking ≥ 20 mg prednisolone daily for more than 6 weeks or in those with anti-TNF therapy (4:8). In the current series, all the patients with FAP underwent a two-stage RPC. However, 5.6% of the patients in the FAP group have had RPC as a salvage procedure after total colectomy with ileo-rectal anastomosis. In the UC group of the present series, 13% of the patients have had previously elective total colectomy in another surgical unit, while 21.7% of the patients have had a three-stage procedure for severe acute disease. Noteworthy, in the present series, a two-stage RPC was performed in an emergent setting in 2.6% of the patients for UC with severe bleeding.

Gaining length in ileal pouch-anal surgery is sometimes necessary to achieve a tension-free anastomosis, particularly when mucosectomy is performed (24). An S pouch might be an alternative to the J pouch to allow a tension-free ileal pouch-anal anastomosis (24). In the present series, 18.2% of patients required the use of lengthening techniques of the mesentery to allow a tension-free ileal pouch-anal anastomosis (all patients have had FAP and associated mucosectomy).

For patients with FAP, mucosectomy appears to be mandatory to completely remove the potential source of rectal adenomas, while for the UC patients a maximum length up to 2 cm ano-rectal mucosa can be left in place (4). Mucosectomy is sometimes technically challenging and might impair the functional results after RPC (25). Furthermore, it appears that the elimination of mucosectomy during RPC for patients with UC is associated with better results in low volume centers (26). In the present series, mucosectomy was performed in all patients with FAP and 47.8% of patients with UC. However, in the last ten years, no mucosectomy was performed for UC patients of the present series (data not shown).

The J-shape pouch is the most frequently performed pouch because it is simple and associated with excellent long-term functional outcomes (8,20,27). No differences between the different pouch designs were observed regarding the small-bowel obstruction, anastomotic leak-age, and pelvic sepsis and wound infection rates (27,28). In the present series, a J pouch was performed 93.5% of the patients. An S pouch is used mainly when there is a problem getting a J pouch to reach the anus for anastomosis (20), as it was the case in the present series.

A double-stapled ileal pouch-anal anastomosis appears to be associated with better functional outcomes, compared with the hand-sewn anastomosis (8,29). Furthermore, few studies have associated hand-sewn anastomosis with higher rates of infectious complications after RPC, compared with the double-stapled technique (30). In the present series, a hand-sewn ileal pouch-anal anastomosis was performed in 81.8% of the patients, while a double-stapled anastomosis was used only 18.2% of the patients. The use of double-stapled ileal pouch-
anal anastomosis was significantly higher in the UC group of patients, compared with the FAP group (52.2% vs. 1.9%, p < 0.001).

A diverting ileostomy is widely recommended for patients with RPC because it may reduce the ileo-anal leakage rate (4,8,20). In the present series, a diverting ileostomy was performed in 92.2% of the patients.

The estimated blood loss in the present series is comparable with data reported in high volume centers worldwide (20).

RPC is a technically challenging surgical procedure, and it is widely accepted to have high morbidity rates. Early morbidity rates reported in high volume centers for RPC are 25.6 – 46.5%, with pouch-related septic complications rates of 12.8 – 20% (Fig. 11), small-bowel obstruction rates of 6.6 – 30% (Fig. 12), wound infections rates of 7 – 10.7%, and hemorrhagic complications rates of 3.3 – 7.4% (8;18;20:30:31). In the present series, the overall early morbidity rate was 36.4%, the pouch-related septic complications rate was 18.2%, wound infections rate was 9.1%, small-bowel obstruction rate was 6.5%, and hemorrhagic complications occurred in 6.5% of the patients. It is recommended that the RPC be performed in referral surgical centers with high-volume of such surgical procedures (4,8). Increased experience is associated with better management of postoperative complications after RPC (19).

**Figure 11.** Computed tomography showing a pelvic abscess (arrow) after RPC (A) coronal plane; (B) sagittal plane, which was percutaneously drained (C) (J – pouch)

**Figure 12.** (A) Contrast-enhanced computed tomography showing small-bowel obstruction after RPC (arrow marks dilated small bowels); (B) Contrast enema of the J pouch showing a reservoir leakage (arrows)
The cut-off to define a low, medium and high volume surgical center and surgeon case-load for RPC remains a matter of debate. The current European Crohn’s and Colitis guidelines for UC recommend that RPC should be performed in surgical centers with at least ten procedures per year (8).

A research performed in the UK in 2011, has categorized both institutional volume and surgeon case-load (16). Thus, a low volume institution is defined as 0.1 – 3.3 RPC/ year or 1 – 39 performed RPC, a medium volume institution is defined as 3.3 – 8.3 RPC/ year or 40 – 100 performed RPC, and a high volume is defined as ≥ 8.4 RPC/ year or ≥ 101 performed RPC (16). For surgeon case-load, the cut-off is the following: 0.1 – 1.3 RPC/ year or 1 – 10 performed RPC (for low volume), 1.4 – 3.5 RPC/ year or 11 – 28 performed RPC (for medium volume), and ≥ 3.6 RPC/ year or ≥ 29 performed RPC (for high volume) (16). According to the abovementioned criteria, our center can be classified as medium volume center, but the surgical team was performing the RPC of the present study as a high case-load.

No significant differences of 30-day mortality rates were observed between low, medium and high volume surgical centers/ surgeons for RPC in a UK national study (16). However, significantly longer hospital stays were observed in the group of low and medium volume centers/ surgeons, compared with the high volume centers/ surgeons (16).

In-hospital mortality rates after RPC varies between 0% and 4% depending on the center volume (32). In the present series, the mortality rate was 1.3%.

Interestingly, a UK national study analyzing the RPC performed between 1996 and 2008 has shown that 91.4% of consultant surgeon teams carried out 20 or fewer RPC, while the median surgeon volume was 4 RPC (16). Furthermore, in a French national study, 89% of the included surgical centers performed less than 3 RPC per year (32).

Conclusions

Although a RPC remains an uncommon surgical procedure in Romania, however, the early outcomes of the present series are comparable to those reported in high volume centers. Good outcomes after RPC can be obtained if such complex surgical procedures are performed by dedicated surgical teams, with high case-load.

Conflict of Interest

The authors declare no conflicts of interests.

References


