Sphincter saving and abdomino-perineal resections following neoadjuvant chemoradiation in locally advanced low rectal cancer

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Abstract  Background: The improvement in surgical techniques alongside neoadjuvant chemoradiation enabled more patients with low rectal cancer to have sphincter preservation.
Study aim: To compare the oncologic and functional outcome in patients with locally advanced low rectal cancer treated by neoadjuvant chemoradiation followed by sphincter saving resection (SSR) against those who underwent abdomino-perineal resection (APR).
Patients and methods: A total of 111 patients with low rectal cancer were included in the study. Sixty-one consented patients who prospectively underwent SSR, from Jan 2008 to Jan 2013, and a retrospective group, formed of 50 patients, selected from cases seen at NCI, with comparable demographic, clinical and pathologic criteria, who underwent APR from Jan 2003 to Jan 2008. All lesions were < 5 cm from anal verge. All 111 patients received preoperative chemoradiation and total mesorectal excision.
Results: All tumors were located at a median of 3.6 cm (range 2.5–4.5 cm) for the SSR group, and 3.5 cm (range 2.5–4.6 cm) for the APR group, from the anal verge. The median follow-up was 34 months (range 1–60 months) for both groups. The difference in disease recurrence and OS between the APR and SSR groups were both statistically insignificant.
Conclusion: In low rectal cancer, the sphincter preservation appears to have nearly the same oncologic outcome compared to APR, this might be attributed to the small sample size and short follow up period. However, patients with sphincter preservation have certainly demonstrated an indisputable better functional outcome, in terms of stoma avoidance and adequate continence.

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Introduction

The standard surgical treatment for rectal adenocarcinoma located up to 5 cm from the anal verge is abdominoperineal resection (APR) [1]. Nowadays, the improvement in functional outcome is a third goal, after overall survival and disease-free survival [2], as the functional result and quality of life of patients who suffer from colorectal cancer has become part of the primary treatment and is being assessed together with the oncologic outcomes. Engel et al. [3] reported that patients with stoma have low self-esteem, altered body image and decreased sexual and physical activity when compared to the others. Thereby, sphincter-preserving operations for lower rectal cancer are becoming more common with the introduction of improved surgical techniques, the use of preoperative concurrent chemoradiation therapy (CCRT), and the realization that a distal resection margin of 1 cm is sufficient to achieve curative resection in most patients [4–7]. However, limitations to the application of SSR are mainly the result of technical difficulties, in addition to oncological considerations: the proximity to, or direct involvement of, the anal sphincter or the levator ani. Accordingly, all the advances, a subset of these patients continues to require abdominoperineal resection [2]. The aim of this study was to explore the possible advantages of the sphincter saving resection (SSR) in patients with locally advanced low rectal cancer treated by neoadjuvant chemoradiation, over the standard abdomino-perineal resection (APR), in terms of postoperative continence, overall survival and disease recurrence.

Patients and methods

A total of 111 patients with low rectal cancer were included in the study. Sixty-one consented patients prospectively underwent sphincter saving resections (SSR). The sample was selected in such a way to detect a medium effect size, with an 80% power and 5% error from January 2008 to January 2013. A retrospective group, of 50 patients, was selected from cases seen at NCI with comparable demographic, clinical and pathologic criteria who underwent APR from January 2003 to January 2008. Patients preoperative enrollment evaluation included liver and kidney function tests, complete blood picture, serum CEA level, digital chest and abdomen erect plain X-rays, endoscopic transrectal ultrasound (ETRUS), abdominopelvic CT with double contrast, colonoscopy with biopsy. Tumor staging was done according to the TNM stage. All patients had low rectal cancer within 5 cm from the anal verge, had locally advanced stage (IIb–III), and received long course of neoadjuvant chemo-radiation (50.4 Gy/28 fractions, and concurrent chemotherapy). Fast track preparation was adopted for new patients. Patients who were not amenable to SSR after the neoadjuvant chemo-radiation underwent abdominoperineal resection and were excluded from the study.

Surgical technique

Different techniques of sphincter preservation were used depending of the site of the tumor. It is important, here, to remember that the resection with a 1 cm longitudinal macroscopic margin should always be the minimum goal in these resections [1]. The rectum was always mobilized off the sacrum using sharp dissection along the parietal fascia, ensuring en-bloc resection of the mesorectum (TME), according to the technique proposed by Heald [8]. Different techniques were used as follows:

- **Low anterior resection (LAR) and colo-anal anastomosis:** For tumors 1 cm, or more, proximal to the dentate line, a classic low anterior resection took place. The colo-anal anastomosis was done manually, or using a circular stapler after resection was done using a straight stapler, and anastomosis was completed by the “double stapling technique” (Fig. 1).

- **Transanal resection and pull-through anastomosis:** For tumors within the anal canal, full resection of the inner sphincter was undertaken with pull-through of the proximal colon, to be anastomosed at the distal edge of the external sphincter.

- **Intersphincteric resection (ISR):** Three types of ISR were used, namely: total, subtotal, and partial. When inevitable, due to tumor spread beyond the dentate line, total ISR was completed by fully excising the internal sphincter, so that the distal margin of the resection is at the intersphincteric groove. In few cases, where the distal edge of the tumor was more than 2 cm far from dentate line, subtotal ISR was performed, getting the distal resection margin between the dentate line and the intersphincteric groove. Preferably, when otherwise enough distal surgical margin existed, distal resection was performed, at or above,
the dentate line, named partial ISR. Dissection was continued through intersphincteric plane till reaching the abdomen dissection level (Fig. 2) [9]. A straight colo-anal hand-sewn anastomosis was done to all the ISR patients, and few of the LAR patients.

In all cases, lateral lymph node dissection (LND) and pelvic autonomic nerve preservation (PANP) were carried out in persisting T3 patients whom MRI pelvic examination revealed nodal diameter >5 mm with heterogeneous pattern. Frozen-section examination was used to confirm the lack of tumor cells in the distal margin. A de-functioning stoma was done for all preoperatively irradiated patients and in those with very low tumors.

Postoperative treatment

Postoperatively, chemotherapy and/or radiotherapy were offered to all indicated patients. All T3 patients received neoadjuvant chemoradiation with or without adjuvant chemotherapy. Patients were followed up until the end of 2012. For the first 2 years, patients were reviewed every 3 months for clinical examination, CEA. Abdomino-pelvic US and CXR were done every 6 months. CT chest, and abdomino-pelvic MRI with full colonoscopy were carried out on annual basis. PET-CT was done to investigate any suspicious findings during the regular follow up protocol. The following 3 years, patients were checked every 6 months then annually thereafter.

Statistical methods

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 17. Comparison between the age of the two groups was done using the Student-t test. Categorical data were compared using Chi-square test. Overall Survival (OS) time was calculated from the date of diagnosis to date of death or last follow-up. The recurrence time was calculated from the date of operation to the date of recurrence, or death. OS and recurrence time were estimated using the methods of Kaplan and Meier. Differences between survival curves were assessed for statistical significance with the log-rank test. All p-values are two-sided. P-values < 0.05 were considered significant.

Results

In this study all tumors were located at a median of 3.6 cm (range 2.5–4.5 cm) for the SSR group, and 3.5 cm (range 2.5–4.6 cm) for the APR group, from the anal verge. Patient’s characteristics are detailed in table 1.

Surgical procedures

All patients received preoperative chemoradiation and total mesorectal excision. The different surgical procedures undertaken are detailed in table 2, with the pictures of removed specimen shown in Fig. 3. Most patients with LAR had either hand-sewn or DST anastomosis; while patients with anorectal resection had hand-sewn colo-anal pull-through anastomosis. Only three patients with coincidental familial polyposis had total proctocolectomy with ileo-anal J-pouch reconstruction.

Oncologic outcome

Circumferential margin (CRM) status, in both groups, and its impact on outcome are detailed in Table 3.

With a median follow up of 34 months (range 1–60 months), for each group, there were 7 and 10 local recurrences among sphincter preservation and APR patients, respectively; while local recurrences occurred in a total of 12
patients; 5 in sphincter preservation and 7 in APR patients. The difference in disease recurrence (Fig. 4) and OS (Fig. 5) between the APR and SSR groups were both statistically insignificant \((p = 0.107,\) and \(0.948,\) respectively) (see Table 4). Continence outcome for patients with sphincter preserving resections (SSR), at 12 months after SSR, and after covering colostomy closure is presented in Table 5.

### Discussion

The oncological and functional outcomes of SSR were dramatically changed by the recognition of the importance

### Table 3  CRM involvement impact on outcome.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CRM Negative</th>
<th>CRMP Positive</th>
<th>(p)-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery type</td>
<td>CRM Negative</td>
<td>CRM Positive</td>
<td>(p)-Value</td>
</tr>
<tr>
<td>SSR ((n = 61))</td>
<td>48 78.7%</td>
<td>13 21.3%</td>
<td>0.134</td>
</tr>
<tr>
<td>APR ((n = 50))</td>
<td>33 66.0%</td>
<td>17 34.0%</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td>CRM Negative</td>
<td>CRM Positive</td>
<td>(p)-Value</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>APR ((n = 50))</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Intraoperative tumor perforation</td>
<td>3 2.7%</td>
<td>8 7.2%</td>
<td></td>
</tr>
</tbody>
</table>

CRM, circumferential margin; SSR, sphincter saving resections; APR, abdomino-perineal resection.

### Table 4  Sphincter preserving resections (SSR) and abdomino-perineal resection (APR) oncologic outcome:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Groups</th>
<th>Number of cases</th>
<th>Number failed</th>
<th>3 years</th>
<th>(p)-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival (OS)</td>
<td>APR 50</td>
<td>6</td>
<td>84.9</td>
<td>0.948</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SSR   61</td>
<td>7</td>
<td>85.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease recurrence</td>
<td>APR 50</td>
<td>14</td>
<td>33.8</td>
<td>0.107</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SSR   61</td>
<td>9</td>
<td>18.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Functional outcome.
of circumferential margin involvement. Once it was discovered that cancer initially spreads laterally into the mesorectum, the priority of operations for mid and low rectal cancers became total mesorectal excision (TME) [8]. Fucini et al. [10] reported that selected patients with very low-lying rectal cancers and responding to preoperative chemoradiation could still be treated with an advanced sphincter-sparing procedure instead of APR with satisfactory oncologic and functional results.

In this study we report 3.6% and 11.7% local recurrences in CRM-negative and CRM-positive APR cases, respectively, comparable to the 5% and 14.9–23.8% reported by other authors [11–13]. The higher rates of one of these studies can be explained by their longer duration of follow-up reaching up to 10 years, and the fact that it included all APR cases done in their institution, not surgically selected “curative” cases.

In this study, the authors also report a CRM-positive in 21.3% of SSR patients with a local recurrence rate of 8.2%, compared to 5–11% and 2%, respectively, reported by other authors [14,15]. Since, the latter two studies concentrated on low rectal tumors and used long-course preoperative radiotherapy, this difference relates most probably to a learning curve that affected the first cases in our study, leading to a higher CRM-positive rate and consequently higher recurrence rates.

We report in this study 11/111 (9.9%) cases, with both resection techniques, of tumor perforation during dissection, all of which in cases with anterior located lesions. Though we restored the integrity of the margins during dissection, specimen examination showed 3 (2.7%) cases with CRM-negative and 8 (7.2%) with CRM-positive specimen, but all of them developed local recurrences later on. This correlates with a number of studies that have demonstrated improvements in local recurrence with a negative CRM (C1–2 mm) [11,12,16–19].

However, in this study, the 3 year recurrence rate at the SSR patient group (18.0%), compared to the APR group (33.8%) was not statistically significant ($p = 0.107$), which coincides with other authors findings [5,13,20–24] who reported better oncolgic outcome for SSR. Alternatively, other researchers [25,26] also reported that the type of resection (AR versus APR) did not influence the risk of local recurrence in lower rectal cancer if surgery was optimized. In general, the evidence appears to suggest that local recurrence is a reflection of the initial tumor biology (stage, histologic grade, and lymphovascular invasion) rather than the type of operative procedure initially performed [27,28]. Nevertheless, one should not overlook the possible impact of the small size of this study sample, and relative short duration of follow up.

In this study, with both groups of patients having comparable clinical, demographic and pathologic criteria, this study reports a 3 year OS, between patients in whom the sphincter was preserved compared to those who underwent APR, of 85.4% and 84.9%, respectively, which are comparable to other studies [13,15,24,29] who reported a 5 years overall survival of 65.8–82%, and 52.3–62.9%, respectively, likely reflecting patient, biologic, and treatment-related factors [15], this also supports the reported improvement of OS with sphincter preservation following preoperative chemoradiation [30].

Since, the choice between the different techniques of SSR was based, not only on the conventional distance between the tumor and the anal verge, or the anorectal ring, but also by infiltration or not of the internal anal sphincter, as well as by the presence of other tumors within the rest of the colon, we were not capable to recruit relatively equal numbers of patients from each technique group; consequently, we could not evaluate, statistically, the results of the separate sphincter preservation techniques.

Regarding the impact of the different levels of low rectal tumors on local recurrence, Rulier et al. [31] classified patients with low rectal cancer (<6 cm from anal verge) into 4 types: type I (supra-anal tumors: >1 cm from anal ring) and these had coloanal anastomosis, type II (juxta-anal tumors: <1 cm from anal ring) and they had partial intersphincteric resection, type III (intra-anal tumors: internal anal sphincter invasion) and these had total intersphincteric resection, and type IV (transanal tumors: external anal sphincter invasion) and they had abdominoperineal resection. They reported no difference in local recurrence (5–9% vs 6%), distant recurrence (23% vs 23%), and disease-free survival (70–73% vs 68%) at 3 years between ultra-low (types II–III) and conventional (type I) sphincter-preserving surgery. Predictive factors of survival were tumor stage and CRM-negative but not the type of tumor or type of surgery [15,31].

The short period of 3 years follow-up time may have given potential for detection and follow-up time bias for the identification of local recurrences that may have been delayed by use of adjuvant radiation. The relatively small number of surgeons allowed for standardization of technique and surgical quality control.

According to Kirwan et al. [32], the present study demonstrates, that SSR showed, at 12 month postoperatively, a perfect (Grade V) functional outcome in 72.1%, and gas incontinence (Grade IV) in 19.7%, comparable to other studies reporting 64.3% and 14.2%, respectively [2]. Only 8.2% of patients experienced major fecal leak (Grade II), especially at night.

**Conclusion**

In low rectal cancer, the sphincter preservation appears to have nearly the same oncologic outcome compared to APR, this might be attributed to the small sample size and short follow up period. It might also be due to the impact of the initial tumor biology (stage, histologic grade, and lymphovascular invasion) which was not tackled in this study. However, patients with sphincter preservation have certainly demonstrated an indisputable better functional outcome, in terms of stoma avoidance and adequate continence.

**Table 5** Sphincter preserving resections (SSR) continence outcome, at 12 months after SSR, and after covering colostomy closure:

<table>
<thead>
<tr>
<th>Continece outcome (Kirwan Grading Scale)</th>
<th>No ($n = 61$)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfect</td>
<td>44</td>
<td>72.1</td>
</tr>
<tr>
<td>Incontinence with flatus</td>
<td>12</td>
<td>19.7</td>
</tr>
<tr>
<td>Accidental feces soiling</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Frequent major soiling</td>
<td>5</td>
<td>8.2</td>
</tr>
<tr>
<td>Anal incontinence</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

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Conflict of Interest

The author denies any actual or potential conflict of interest; financial or otherwise.

References